NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Glofitamab for treating relapsed or refractory B-cell lymphoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of glofitamab within its marketing authorisation for treating relapsed or refractory 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 DLBCL (transformed high grade follicular lymphoma). Subsets of DLBCL include high grade B-cell lymphoma (HGBCL) which is an aggressive form of the disease associated with specific genetic changes and primary mediastinal large B-cell lymphoma (PMBCL) which develops when abnormal B-cells develop in the thymus gland and accumulate in the lymph nodes behind the breast-bone (mediastinum). The symptoms of DLBCL 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 (extra-nodal 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] Most people diagnosed with DLBCL are 65 years or over.[2] Survival rate at 5 years for DLBCL is around 60%.[3] Although most patients are cured with first-line chemotherapy, about 10-15% have primary refractory disease and a further 20-30% relapse.

The most widely used first-line treatment for DLBCL is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone), which may be followed by radiotherapy. Sometimes etoposide is added to this regimen. NICE guideline NG52 recommends multi-agent chemotherapy in combination with rituximab for relapsed or refractory disease potentially 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.

For those with relapsed or refractory DLBCL, the following treatments are recommended by NICE:

- NICE technology appraisal 649 recommends polatuzumab vedotin with rituximab and bendamustine for adults who cannot have a haematopoietic stem cell transplant.
- NICE technology appraisal 567 recommends tisagenlecleucel within the CDF for adults whose DLBCL is relapsed or refractory to two prior systemic treatments.
- NICE technology appraisal 559 recommends axicabtagene ciloleucel within the CDF for adults whose DLBCL is relapsed or refractory to two prior systemic therapies.
- NICE technology appraisal 306 recommends pixantrone monotherapy for adults whose non-Hodgkin B-cell lymphoma requires third or fourth line treatment and who have previously been treated with rituximab.

The technology

Glofitamab (brand name unknown, Roche) does not currently have a marketing authorisation in the UK. It is being studied in a clinical trial as a monotherapy and in combination with obinutuzumab in adults with B-cell non-Hodgkin lymphoma which is relapsed or refractory to at least one prior treatment.

Intervention(s)	Glofitamab
Population(s)	Adults with relapsed or refractory B-cell Lymphoma

Comparators	• established clinical management without glofitamab, including but not limited to:
	• chemotherapy with or without rituximab and with or without stem cell transplantation, 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 monotherapy
	• axicabtagene ciloleucel (subject to NICE evaluation)
	• tafasitamab with lenalidomide (if haematopoietic stem cell transplantation is not possible and 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 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 (2020) NICE Technology Appraisal 649. Tisagenlecleucel for treating relapsed or refractory diffuse large B-cell lymphoma after 2 or more systemic therapies (2019) NICE Technology Appraisal 567. 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. Pixantrone monotherapy for treating multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma (2014, Reviewed March 2021) NICE Technology Appraisal 306. **Appraisals in development:** Tafasitamab with lenalidomide for treating relapsed or refractory diffuse large B-cell lymphoma NICE technology

	appraisals guidance [ID3795] Publication expected October 2022 **Related Guidelines:** "Haematological cancers: improving outcomes" (2016) NICE guideline 47. "Non-Hodgkin's lymphoma: diagnosis and management" (2016, Updated October 2021) NICE guideline 52. Review date to be confirmed "Non-Hodgkin's lymphoma: rituximab subcutaneous injection" (2014) NICE evidence summary 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 (2018/2019) NHS manual for prescribed specialist services (2018/2019) – Chapters 29 and 105 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 -5 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for glofitamab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for B-cell lymphoma?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom glofitamab is expected to be more clinically effective and cost effective or other groups that should be examined separately? OR Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom glofitamab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider glofitamab will fit into the existing care pathway?

The trial gave glofitamab after a loading dose of obinutuzumab. Is this how the drug would be used in NHS clinical practice?

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 glofitamib 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 glofitamab 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 glofitamab 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. NHS Digital. Cancer Registration Statistics, England 2019. (2021) Accessed February 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. Non-Hodgkin Lymphoma - Survival (2022) Accessed February 2022.

4. Haematological Malignancy Research Network (HMRN) data (2004-2016) Accessed February 2022.

