NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Polatuzumab vedotin in combination for untreated diffuse large B-cell lymphoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of polatuzumab vedotin with R-CHP (rituximab, cyclophosphamide, doxorubicin, and prednisolone) within its marketing authorisation for untreated 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 are two biologically distinct subtypes of DLBCL, germinal centre B-cell (which arises in secondary lymphoid organs such as lymph node and spleen) and post-germinal centre (also known as activated B-cell lymphoma) which differ in prognosis. They are distinguished by immunohistochemical testing of gene expression profiling.

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].

Overall survival rates at 5 years for DLBCL were around 55.4% in 2004-2011[3]. However, diagnosis at early stage and post-germinal DLBCL have a better prognosis. Survival rates at 5 years were around 63.5-70.1% for stage I and II and around 51.8-46.2% for stages III and IV[3]. Current first-line treatment is combination chemotherapy with rituximab. The most widely used first-line chemoimmunotherapy is R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone). Sometimes etoposide is added to

this regimen or doxorubicin is substituted with a different treatment (such as gemcitabine, etoposide or liposomal doxorubicin). In addition, R-ACVBP (rituximab, doxorubicin, vindesine, cyclophosphamide, bleomycin and prednisolone) can be used instead of R-CHOP[4]. NICE guideline NG52 recommends central nervous system-directed prophylaxis for some people.

The technology

Polatuzumab vedotin (Polivy, Roche) is an antibody drug conjugate which is a monoclonal antibody combined with a cytotoxic agent called monomethyl auristatin E (MMAE). It acts by selectively binding to CD79b, a protein which is found on the surface of B-cells, resulting in the death of B-cells. It is administered as an intravenous infusion.

Polatuzumab vedotin with R-CHP does not currently have a marketing authorisation in the UK for untreated DLBCL. It has been studied in clinical trials in which polatuzumab vedotin and R-CHP chemoimmunotherapy was compared to R-CHOP chemoimmunotherapy, in adults with DLBCL who have not received prior treatment.

Intervention(s)	Polatuzumab vedotin with R-CHP (rituximab, cyclophosphamide, doxorubicin, and prednisolone)
Population(s)	Adults with untreated diffuse large B-cell Lymphoma
Comparators	Chemoimmunotherapy (including R-CHOP)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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 and cost of biosimilars should be taken into account.
Other considerations	If the evidence allows the following subgroups will be considered. These include: • germinal centre DLBCL, and • post-germinal centre DLBCL 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. The availability and cost of biosimilar products should be taken into account.
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 guidance 649 Related Guidelines: Non-Hodgkin's lymphoma: diagnosis and management (2016) NICE Guideline NG52 Related Quality Standards: Haematological cancers (2017) NICE Quality Standard 150 Related NICE Pathways: Non-Hodgkin's lymphoma overview (2018) 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, specialist cancer services (adult)

	Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

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

Would polatuzumab vedotin only be given with R-CHP or would it be also considered in combination with other chemoimmunotherapy? If so what chemoimmunotherapy would be used?

What tests are used to diagnose DLBCL?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom polatuzumab vedotin with R-CHP is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider polatuzumab vedotin will fit into the existing NICE pathway, non-Hodgkin's lymphoma?

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 polatuzumab vedotin with R-CHP 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 polatuzumab vedotin with R-CHP 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 polatuzumab vedotin with R-CHP 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. Lymphoma association. Diffuse Large B-cell lymphoma. Accessed September 2021.

3. Cancer Research UK. Haematological Malignancy Research Network (HMRN) data (2004-2011) Non-Hodgkin lymphoma survival statistics Accessed October 2021.

4. Tilly H, Silva M, Vitolo U et al. (2015) Diffuse large B-cell lymphoma (DLBCL): ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Annals of Oncology ;26(Suppl 5):v116-v125.