NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Lenalidomide with rituximab for untreated follicular lymphoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of lenalidomide with rituximab within its marketing authorisation for untreated follicular lymphoma.

Background

Lymphomas are cancers of the lymphatic system, which is part of the body's immune system. They are divided into Hodgkin's and non-Hodgkin's lymphomas. Non-Hodgkin's lymphomas are a heterogeneous group of conditions ranging from 'indolent' (low-grade) to 'aggressive' (high-grade) depending on the rate at which the abnormal lymphocytes divide. Indolent lymphomas are slow growing, with long median survival times but are less likely to be cured by treatment. Follicular lymphoma is the most common type of indolent non-Hodgkin's lymphoma. Patients with follicular lymphoma typically present with painless, swollen lymph nodes in the neck, armpit or groin. Lymphomas are commonly staged I (best prognosis) to IV (worse prognosis). The stage of the lymphoma reflects how many groups of lymph nodes are affected, where they are in the body, and whether other organs such as the bone marrow or liver are affected. Most people (80%) present with advanced disease (stage III to IV).

In 2015, approximately 11,700 people were diagnosed with non-Hodgkin's lymphoma in England, of whom around 20% had follicular lymphoma.[1,2] The 5-year survival rate for people with follicular lymphoma is 87% and 20-year survival rates have been reported to be as high as 44%.[3]

NICE technology appraisal guidance 243 recommends rituximab in combination with chemotherapy as an option for untreated symptomatic stage III and IV follicular lymphoma. NICE technology appraisal guidance 513 recommends obinutuzumab for people who have a Follicular Lymphoma International Prognostic Index of 2 or more in combination with chemotherapy, followed by obinutuzumab maintenance therapy. For people who do not have symptoms, the NICE clinical guideline for non-Hodgkin lymphoma recommends that rituximab is given alone, although at the time of writing this draft scope rituximab monotherapy did not have a marketing authorisation in the UK for untreated non-Hodgkin lymphoma.

For people whose follicular non-Hodgkin lymphoma has responded to first-line induction therapy with rituximab in combination with chemotherapy, NICE technology appraisal guidance 226 recommends rituximab maintenance therapy as an option. People whose disease does not respond to treatment, or relapses after treatment is completed, will usually receive a different

combination chemotherapy regimen, with or without rituximab. Stem cell transplantation may also be considered.

The technology

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

Rituximab (MabThera, Roche Products) is a genetically engineered chimeric (mouse/human) monoclonal antibody that depletes B cells by targeting cells bearing the CD20 surface marker. It is administered intravenously.

Lenalidomide with rituximab does not currently have a marketing authorisation in the UK for untreated follicular lymphoma. It is currently being studied in a clinical trial, compared with rituximab with chemotherapy (CHOP, CVP, or bendamustine), in adults with untreated follicular lymphoma.

Intervention(s)	Lenalidomide with rituximab
Population(s)	People with untreated advanced follicular lymphoma
Comparators	• Rituximab monotherapy (does not currently have a marketing authorisation in the UK for this indication) • Rituximab in combination, with or without rituximab maintenance treatment • Obinutuzumab in combination, followed by obinutuzumab maintenance treatment (for people with a Follicular Lymphoma International Prognostic Index [FLIPI] score of 2 or more)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • overall 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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 patient access schemes for the intervention or comparator technologies will be taken into account. The availability and cost of biosimilar products should be taken into account.
Other considerations	If evidence allows, consideration will be given to subgroups based on Follicular Lymphoma International Prognostic Index score (FLIPI). 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**: Rituximab for the first-line treatment of stage III-IV follicular lymphoma (2012) NICE Technology Appraisal 243. Review decision August 2014: static guidance list. Rituximab for the first-line maintenance treatment of follicular non-Hodgkin's lymphoma (2011) NICE Technology Appraisal 226. Review decision August 2014: static guidance list. Obinutuzumab for untreated advanced follicular lymphoma (2018) NICE Technology Appraisal 513. Review date: March 2021 **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. **Related NICE Pathways** Non-Hodgkin's lymphoma (2016) NICE pathway
Related National Policy	Department of Health, NHS Outcomes Framework 2016-2017, Dec 2016. Domains 1, 2, 4 and 5. NHS England, National Cancer Drugs Fund List, Accessed May 2018. NHS England, Manual for prescribed specialised services 2016-2017, May 2016. Chapters 105 and 106 (specialist cancer services, adults and children). Department of Health, Improving Outcomes: A strategy for cancer, fourth annual report, Dec 2014. Independent Cancer Taskforce Achieving world-class cancer outcomes: a strategy for England 2015-2020 July 2015

Questions for consultation

Have all relevant comparators for lenalidomide with rituximab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for untreated advanced follicular lymphoma?

Is bendamustine or rituximab monotherapy considered to be established clinical practice in the NHS for untreated advanced follicular lymphoma?

Are the outcomes listed appropriate?

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

Where do you consider lenalidomide with rituximab 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 lenalidomide with rituximab 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 lenalidomide with rituximab 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 lenalidomide with rituximab 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 technologies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1 Cancer Research UK (2013) Non Hodgkin lymphoma incidence statistics. Accessed May 2017

2 Haematological Malignancy Research Network (2014) HMRN Incidence Accessed May 2017

3 Cancer Research UK (2004–11) Non Hodgkin lymphoma survival statistics. Accessed May 2017