**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

# Proposed Health Technology Appraisal

# Obinutuzumab in combination with bendamustine for treating rituximab-refractory follicular lymphoma

## Draft scope (pre-referral)

### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of obinutuzumab in combination with bendamustine within its marketing authorisation for treating rituximab-refractory 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 lymphoma includes a number of different conditions, which may be classified based on their grade (how fast they grow) or type (the characteristics of the cancer cells). Low-grade, or 'indolent' non-Hodgkin's lymphomas are slow growing, and often have long survival times but low cure rates; follicular lymphoma is one of the most common types of indolent non-Hodgkin's lymphoma.

In 2012, approximately 10,900 people were diagnosed with non-Hodgkin's lymphoma in England,[1] of whom approximately 17–19% have follicular lymphoma.[1,2] Approximately 87% of people with follicular lymphoma survive for 5 years or more.[3]

Most people with advanced follicular lymphoma will have initial treatment with chemotherapy in combination with rituximab, often followed by maintenance therapy with rituximab. However, most people's lymphoma will relapse after the initial response, and treatment is often characterised by multiple lines of treatment as the disease responds and relapses. Cancers that do not respond to rituximab are termed 'rituximab refractory'. Treatment options for rituximab-refractory follicular lymphoma include single- or multi-agent chemotherapy (for example, including cyclophosphamide, fludarabine, bendamustine or chlorambucil) and best supportive care.

### The technology

Obinutuzumab (Gazyva, Roche Products) is a type 2 glycoengineered antibody that binds to the CD20 protein present on B cells, except stem or plasma cells, and causes cell death. It is administered by intravenous infusion.

Obinutuzumab does not currently have a marketing authorisation in the UK for treating non-Hodgkin's lymphoma. It has been studied in combination with

bendamustine, compared with bendamustine alone, for treating adults with rituximab-refractory indolent non-Hodgkin's lymphoma.

| | |
|---|---|
| **Intervention(s)** | Obinutuzumab in combination with bendamustine |
| **Population(s)** | People with follicular lymphoma that is refractory to rituximab or rituximab-containing regimens |
| **Comparators** | • Chemotherapy regimens with or without rituximab<br>• Best supportive care |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• overall response rate<br>• duration of response/remission<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>Biosimilars are not expected to be in established NHS practice at the time of appraisal and are not included as comparators. |
| **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:<br>'Idelalisib for treating follicular lymphoma that is refractory to 2 prior treatments' (terminated appraisal; 2014). NICE Technology Appraisal 328. |

| | |
|---|---|
| | 'Bendamustine for the treatment of indolent (low grade) non-Hodgkin's lymphoma that is refractory to rituximab' (terminated appraisal; 2010). NICE Technology Appraisal 206.<br><br>'Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma: Review of technology appraisal guidance 37' (2008). NICE Technology Appraisal 137. Static list.<br><br>Appraisals in development:<br><br>'Bortezomib for the treatment of relapsed or refractory follicular non-Hodgkin's lymphoma' NICE technology appraisals guidance [ID407]. Suspended.<br><br>Related guidelines:<br><br>'Improving outcomes in haematological cancers' (2003) NICE guidance on cancer services. Review in progress, publication date TBC.<br><br>Guidelines in development:<br><br>'Non-Hodgkin's lymphoma: diagnosis and management of non-Hodgkin's lymphoma'. Publication expected July 2016.<br><br>Related NICE Pathways:<br><br>Blood and bone marrow cancers (2015) NICE pathway<br><br>http://pathways.nice.org.uk/ |
| **Related National Policy** | Department of Health (2011) Improving outcomes: a strategy for cancer<br><br>Department of Health (2009) Cancer commissioning guidance<br><br>Department of Health (2007) Cancer reform strategy<br><br>Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domain 1. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf |

## Questions for consultation

Have all relevant comparators for obinutuzumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for rituximab-refractory follicular lymphoma?

- What chemotherapy regimens are commonly used?
- Is rituximab used for rituximab-refractory disease?

- Is idelalisib used in this setting?
- How should best supportive care be defined?

Is high-dose chemotherapy followed by stem-cell transplantation used for people with rituximab-refractory follicular lymphoma?

- If so, should it be included a comparator?
- Should people for whom stem-cell transplantation is suitable be considered as a separate subgroup?

Are there any subgroups of people in whom obinutuzumab is expected to be more clinically effective and cost effective or other groups that should be examined separately? Should consideration be given to subgroups based on the person's previous treatment?

Where do you consider obinutuzumab 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 obinutuzumab 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 obinutuzumab 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 obinutuzumab 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.

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 (2014) Cancer registration statistics, England, 2012. Accessed March 2015.

2. Cancer Research UK (2013) Non-Hodgkin lymphoma incidence statistics. Accessed March 2015.

3. Cancer Research UK (2014) Non-Hodgkin lymphoma survival statistics. Accessed March 2015.