NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Obinutuzumab for untreated advanced follicular lymphoma

Final scope

Remit

To appraise the clinical and cost effectiveness of obinutuzumab within its marketing authorisation for untreated advanced follicular lymphoma.

Background

Lymphomas are cancers of the lymphatic system, which is part of the body's immune system, and involve abnormal production of lymphocytes (a type of white blood cell). They are divided into Hodgkin and non-Hodgkin lymphomas. Non-Hodgkin 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. Follicular lymphoma, which affects B cells, is the most common type of indolent non-Hodgkin lymphoma[1]. People 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. More people are diagnosed with advanced (stage III or IV) non-Hodgkin lymphoma than early stage disease (stage I and II): 50% are diagnosed with advanced disease, 29% are diagnosed with early stage disease, and in the remainder of cases the stage at diagnosis is not known[2].

In 2013, approximately 11,400 people were diagnosed with non-Hodgkin lymphoma in England, of whom around 20% had follicular lymphoma[2]. The 1-year and 5-year survival rates for people with follicular lymphoma are 96% and 87%, respectively[3].

Advanced-stage follicular lymphoma will initially be treated with chemotherapy, usually in combination with rituximab, and radiotherapy. NICE technology appraisal guidance 243 recommends rituximab in combination with cyclophosphamide, vincristine and prednisolone (CVP), cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP), mitoxantrone, chlorambucil and prednisolone (MCP), cyclophosphamide, doxorubicin, etoposide, prednisolone and interferon-α (CHVPi) or chlorambucil as an option for untreated symptomatic stage III and IV follicular lymphoma. 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 does not have a marketing authorisation in the UK for untreated non-Hodgkin lymphoma. In addition, bendamustine (which does not currently have a marketing authorisation in the UK for untreated non-Hodgkin lymphoma) has

been available through the Cancer Drugs Fund, alone or in combination with rituximab, as an option for people with untreated indolent 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

Obinutuzumab (Gazyvaro, Roche Products Limited) is a type II monoclonal antibody which binds to the CD20 cell surface antigen on B cells and causes cell death. It is administered intravenously.

Obinutuzumab does not currently have a marketing authorisation in the UK for untreated advanced follicular lymphoma. It has been studied in clinical trials in combination with chemotherapy as an induction treatment, compared with rituximab in combination with chemotherapy, in adults with untreated, advanced, indolent non-Hodgkin lymphoma (including follicular lymphoma). The clinical trials also assessed maintenance treatment with obinutuzumab or rituximab monotherapy, taken until disease progression or for up to 2 years, for people whose disease responded to induction therapy.

Obinutuzumab in combination with bendamustine, followed by obinutuzumab maintenance therapy, has a marketing authorisation in the UK for treating follicular lymphoma in people whose disease did not respond to, or progressed during or up to 6 months after, treatment with rituximab or a rituximab-containing regimen. A NICE technology appraisal of obinutuzumab in this population is ongoing (ID841).

Intervention(s)	Obinutuzumab in combination with chemotherapy, with or without obinutuzumab maintenance therapy
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-based chemotherapy, with or without rituximab maintenance treatment • Bendamustine monotherapy (does not currently have a marketing authorisation in the UK for this indication; not appraised by NICE but funded via the CDF)

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. 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	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. **Appraisals in development (including suspended appraisals)** Obinutuzumab in combination with bendamustine for treating rituximab-refractory follicular lymphoma NICE technology appraisals guidance [ID841]. Publication date to be confirmed.

	Bendamustine in combination with rituximab for the first-line treatment of indolent non-Hodgkin's lymphoma (suspended appraisal) [ID434]. **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, Sep 2016. 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. Department of Health, Cancer commissioning guidance, Dec 2009.

References

1 Cancer Research UK (2014) Different types of non Hodgkin lymphoma. Accessed September 2016

2 Cancer Research UK (2013) Non Hodgkin lymphoma incidence statistics. Accessed September 2016

3 Cancer Research UK (2004–11) Non Hodgkin lymphoma survival statistics. Accessed September 2016