NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Rituximab for the first-line treatment of stage III-IV follicular lymphoma (Review of TA 110)

Draft scope

Appraisal objective

To appraise the clinical and cost effectiveness of rituximab, within its licensed indication, for the first line treatment of stage III-IV follicular lymphoma (review of existing guidance 110).[1]

Background

Lymphomas are cancers of the lymphatic system. They are broadly divided into Hodgkin's lymphoma and non-Hodgkin's lymphomas (NHL). NHL can be divided into low grade and aggressive lymphomas. Low-grade (also called 'indolent') lymphomas are slow growing, with long median survival times but are less likely to be cured by treatment. Follicular lymphoma is a low-grade lymphoma of B-lymphocytes and accounts for approximately 30% of all low-grade lymphomas.

Precise identification of the type of lymphoma and accurate staging of the disease is crucial both for choosing the optimum treatment and for monitoring disease progression. The stage of NHL 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. One of the most common systems for classifying NHL identifies four stages. Early follicular lymphoma includes stages I and II, and advanced disease includes stages III and IV. In stage I, only one group of lymph nodes in one organ of the body is affected. In stage II, the disease has spread to two lymph groups on the same side of the diaphragm. Stage III disease includes lymph nodes affected on both sides of the diaphragm, and stage IV of the disease usually involves multiple internal organs, for example, the liver, bone marrow, or blood.

NHL accounts for approximately 4% of all cancers diagnosed in the UK, with 9431 new cases registered in England and Wales in 2006, and 4011 registered deaths in 2007. Depending on the classification system used, between 22% and 40% of NHLs are follicular. The incidence of follicular lymphoma increases with age, with the median age at diagnosis between 60 and 65 years. Over 70% of people with follicular lymphoma are still alive 5

[1] The remit from the Department of Health is to appraise the clinical and cost effectiveness of rituximab in combination with other drugs as a first line treatment for low grade non-Hodgkin's lymphoma.

years after the diagnosis, with median survival over 10 years. Most people will have disease at stage III or IV at the time of diagnosis.

For many people, regular check-ups are the most appropriate clinical management (known as active surveillance or watchful waiting), until active treatment is needed when symptoms develop. There may be many episodes of remission and relapse, and the nature of the disease can change at relapse, sometimes transforming to a more aggressive type. Treatment for low-grade NHL can lead to partial remission (decrease the size of the lymphoma, or reduce the extent of lymphoma in the body) or to complete remission (when the disease is not detectable anymore).

The aim of current management is to prolong survival, achieve the longest possible remission and improve quality of life. First-line treatment options for stage III or IV follicular lymphoma include single-agent or combination chemotherapy regimens based on alkylating agents, without or with steroids (chemo-immunotherapy). Rituximab in combination with cyclophosphamide, vincristine and prednisolone (CVP regimen) is recommended in NICE guidance (TA110) as a first-line treatment option for symptomatic stage III or IV follicular lymphoma.

The technology

Rituximab (Mabthera, Roche Products) is a genetically engineered monoclonal antibody that targets the CD-20 surface marker of mature B-cell lymphocytes. This marker is expressed on almost all B-cell lymphomas and testing for its presence is part of the normal diagnostic procedure.

Rituximab has a UK marketing authorisation for the first-line treatment of previously untreated patients with stage III-IV follicular lymphoma in combination with any chemotherapy regimen. This indication has replaced the previous marketing authorisation for rituximab where it was only licensed for use in combination with a specific chemotherapy regimen of cyclophosphamide, vincristine and prednisolone (R-CVP).

Rituximab also has a UK marketing authorisation for maintenance therapy for patients with relapsed/refractory follicular lymphoma responding to induction chemotherapy with or without rituximab. It is also licensed for the treatment of patients with CD20-positive diffuse large B-cell NHL in combination with CHOP chemotherapy, and as monotherapy for patients with stage III-IV follicular lymphoma who are resistant to chemotherapy or are in their second or subsequent relapse after chemotherapy.

Intervention(s)	Rituximab in combination with chemotherapy
Population(s)	Adults with stage III-IV follicular lymphoma who have not received any previous treatment

Comparators	Chemotherapy without rituximab
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.
Other considerations	If the evidence allows, subgroup analyses by type of chemotherapy regimen received will be considered. Guidance will only be issued in accordance with the marketing authorisation
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No 137, September 2008, Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma (review of technology appraisal guidance 37). Technology Appraisal No 110, September 2006, Rituximab for the treatment of follicular lymphoma. Review Date June 2009. Technology Appraisal in Preparation. Rituximab for the maintenance treatment of follicular non-Hodgkin's lymphoma following response to first-line chemotherapy. Earliest anticipated date of publication January 2011.

	Related Guidelines: Clinical Guideline No. CSGHO, October 2003, "Improving outcomes in haemato-oncology cancer".

Questions for Consultation

Have the most appropriate comparators been included in the scope?

Are there any subgroups of patients in whom rituximab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

What do you consider to be the relevant clinical outcomes and other potential health related benefits of rituximab in combination with chemotherapy in the treatment of follicular lymphoma, particularly when compared with currently used treatment options?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?