# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## Health Technology Appraisal

## Rituximab for first line and relapsed chronic lymphocytic leukaemia

## Draft scope (Pre-referral)

### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of rituximab within its licensed indication for the first line treatment of chronic lymphocytic leukaemia
AND
To appraise the clinical and cost effectiveness of rituximab within its licensed indication for the relapsed treatment of chronic lymphocytic leukaemia
(or handled together as an MTA)

### Background

Chronic lymphocytic leukaemia (CLL) is a malignant disorder of white blood cells (lymphocytes). CLL causes abnormal lymphocytes to proliferate, which in turn causes anaemia, failure of the blood to clot and increased susceptibility to infection. CLL often remains undiagnosed either until it is well advanced, or until a chance test shows abnormally high levels of lymphocytes in the blood. It is a chronic and incurable disease. CLL is the most common form of leukaemia in the UK.

In England, 1,961 cases of CLL were diagnosed in 2004. In England and Wales, CCL caused 978 deaths in 2005. Seventy five percent of people diagnosed with CCL are over the age of 60 years, and twice as many men as women are affected. There are two genetic subtypes of CLL, one having a median survival of about 25 years and the other of about 8 years. Life expectancy of both genetic subtypes of CLL depends on the stage at which the disease is diagnosed. Other prognostic factors include age of onset.

People who have early stage disease normally undergo general observation, referred to as ‘watchful waiting’. In people with intermediate or advanced stages of the disease, alkylating agents such as cyclophosphamide (with or without corticosteroids), have been used as a first-line treatment.

### The technology

Rituximab (MabThera, Roche) is a chimeric (mouse/human) genetically engineered monoclonal antibody. It targets the CD-20 surface marker of mature B-cell lymphocytes. It is administered by intravenous infusion.

Rituximab is currently licensed for other indications, but currently has no marketing authorisation for treatment of first line or relapsed CLL. It has been studied in clinical trials with fludarabine monotherapy or fludarabine cyclophosphamide combination therapy for these two indications.

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| **Intervention(s)** | Rituximab (in combination with fludarabine therapies) |
| **Population(s)** | Patients with first-line or relapsed chronic lymphocytic leukaemia |
| **Standard comparators** | First-line<br>• chlorambucil<br>• fludarabine monotherapy (or in combination)<br>Relapsed<br>• chlorambucil<br>• fludarabine monotherapy (or in combination)<br>• cyclophosphamide, doxorubicin, vincristine, prednisone (CHOP) combination therapy<br>• stem cell transplant |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rates<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. |
| **Other considerations** | Guidance will only be issued in accordance with the marketing authorisation. |

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| **Related NICE recommendations** | Related Technology Appraisals:<br>Technology Appraisal No. 29, September 2001, Fludarabine for the treatment of B-cell chronic lymphocytic leukaemia.<br>Technology Appraisal No. 119, February 2007, Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia.<br>Related Guidelines:<br>Cancer Service Guidance, October 2003, Improving outcomes in haemato-oncology cancer.<br>Related Interventional Procedures:<br>None<br>Related Public Health Guidance/Guidelines:<br>None |

**Questions for consultation**

Have the most appropriate comparators for the treatment of first-line and relapsed CLL been included in the scope?

Is stem cell transplant considered an appropriate comparator?

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

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?

Should the appraisal be split into two single technology appraisals (e.g. first-line and relapsed) or appraised as a multiple technology appraisal?

(Information on the single and multiple technology processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)