NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Rituximab for the first line treatment of chronic lymphocytic leukaemia

Final scope

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

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 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. CLL is genetically heterogeneous, but there are two broad subtypes, one having a median survival of about 25 years and the other of about 8 years. Life expectancy of both subtypes of CLL depends on the stage at which the disease is diagnosed. Other prognostic factors include age of onset, spread of disease and response to treatment.

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 chlorambucil (with or without corticosteroids) may be used as a first-line treatment. Fludarabine combination therapies are an alternative first-line treatment option.

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

Intervention(s)	Rituximab (in combination with fludarabine therapies)
Population(s)	Patients with previously untreated chronic lymphocytic leukaemia
Standard comparators	• chlorambucil • fludarabine combination therapy
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	Guidance will only be issued in accordance with the marketing authorisation. If evidence and marketing authorisation allow, the appraisal should consider subgroups based on the following: 53 presence and p53 mutation or deletion.

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