NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Proposed Health Technology Appraisal

Bendamustine for the treatment of chronic lymphocytic leukaemia

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of bendamustine 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.People with symptomatic CLL may experience anaemia and fatigue, as well as enlarged lymph nodes, liver and spleen, bone pain, abnormal bruising, sweating, loss of appetite and reoccurring infections.

In England, 1961 cases of CLL were diagnosed in 2004. In England and Wales, CLL caused 978 deaths in 2005. Seventy five percent of people diagnosed with CLL are over the age of 60 years, and twice as many men as women are affected. CLL is genetically heterogeneous with median survival ranging from about 3 to 12 years depending on the genetic subtype and the stage at which the disease is diagnosed. Other prognostic factors include age of onset, spread of disease and response to treatment.

Treatment options vary depending on factors such as stage of CLL, performance status, co-morbidities and genetic markers. A number of treatments are available that can reduce the tumour burden and improve quality of life. People who have early stage disease or non-symptomatic disease normally undergo general observation, referred to as ‘watchful waiting’. In people with symptomatic disease, fludarabine combination therapy is a commonly used a first-line treatment. However, fludarabine combination therapies are not appropriate for all people with CLL. For people unable to take fludarabine (for example, because of comorbidities or poor performance status) chlorambucil is often used. NICE guidance (TA174) recommends the use of rituximab in combination with fludarabine and cyclophosphamide as a first-line treatment option for people who are able to take fludarabine and cyclophosphamide. It does not recommend the use of other rituximab containing chemotherapies as first-line treatment options. NICE guidance (TA119) does not recommend fludarabine monotherapy as a first-line treatment for people with CLL. The chronic relapsing nature of CLL means

that most people will require more than one treatment episode during the course of their disease. The technology

Bendamustine (brand name unknown, Napp Pharmaceuticals) is a bifunctional mechlorethamine derivative containing a purine-like benzimidazol ring.
The drug is an alkylating antitumour agent which cross links DNA and impairs its synthesis and repair in tumour cells, leading to apoptosis (cell death). It is administered by intravenous infusion.

Bendamustine does not currently have a UK marketing authorisation. It has been studied in clinical trials in comparison with chlorambucil in patients with untreated chronic lymphocytic leukaemia.

Intervention(s)	Bendamustine
Population(s)	People with previously untreated chronic lymphocytic leukaemia for whom fludarabine combination chemotherapy is not appropriate.
Comparators	• Chlorambucil
Outcomes	The outcome measures to be considered include: • progression free survival • response rates • overall survival • 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 evidence allows, the appraisal will consider subgroups of people defined by their: • performance status • stage of disease (Binet B and C) • co-morbidities Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Technology appraisal No.174, June 2009, Rituximab for first-line treatment of chronic lymphocytic leukaemia (expected review date December 2010). Technology appraisal No.119, February 2007, Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia (currently on the static list). Technology appraisal in preparation. Rituximab for the treatment of relapsed/refractory chronic lymphocytic leukaemia. Earliest anticipated date of publication: April 2010. Related Guidelines: Cancer service guidance CSGHO, October 2003, Improving outcomes in haemato-oncology cancer (expected review date TBC).