

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE**Proposed Health Technology Appraisal****Bendamustine for the treatment of chronic lymphocytic leukaemia****Draft scope (Pre-referral)****Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of bendamustine within its licensed indication for the first-line treatment of patients with 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, 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 normally undergo general observation, referred to as 'watchful waiting'. In people with symptomatic disease, fludarabine combination therapies and chlorambucil (with or without corticosteroids), are commonly used as a first-line treatments. 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 technology

Bendamustine (brand name unknown, Napp Pharmaceuticals) is a bifunctional mechlorethamine derivative containing a purine-like benzimidazol ring. The drug and its derivatives break down into alkyl groups which bond

with substances inside tumour cells leading to 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.
Comparators	<ul style="list-style-type: none"> • Fludarabine combination therapies with or without rituximab • Chlorambucil
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • progression free survival • response rates • overall survival • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.

<p>Related NICE recommendations</p>	<p>Related Technology Appraisals:</p> <p>Technology appraisal No.174, June 2009, Rituximab for first-line treatment of chronic lymphocytic leukaemia (expected review date December 2010).</p> <p>Technology appraisal No.119, February 2007, Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia (expected review date October 2009).</p> <p>Technology appraisal in preparation. Rituximab for the treatment of relapsed/refractory chronic lymphocytic leukaemia. Earliest anticipated date of publication: April 2010.</p> <p>Related Guidelines:</p> <p>Cancer service guidance CSGHO, October 2003, Improving outcomes in haemato-oncology cancer (expected review date TBC).</p>
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Questions for consultation

Have the most appropriate comparators for the treatment of bendamustine been included in the scope?

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?

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)