NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single Technology Appraisal

Bendamustine in combination with rituximab for the first-line treatment of mantle cell lymphoma

Draft scope (post-referral)

Remit/appraisal objective

To appraise the clinical and cost effectiveness of bendamustine in combination with rituximab within its licensed indication for the first-line treatment of mantle cell lymphoma.

Background

Lymphomas are cancers of the lymphatic system, which is a part of the body's immune system. Traditionally, lymphomas are divided into Hodgkin's disease (now known as Hodgkin's lymphoma) and non-Hodgkin's lymphoma. Non-Hodgkin's lymphomas are a diverse group of conditions which are categorised according to the cell type affected (B-cell or T-cell), as well as the clinical features and rate of progression of the disease. Mantle cell lymphoma is a rare type of non-Hodgkin's lymphoma affecting the B-cells.

Lymphomas are graded according to the rate at which the abnormal lymphocyte cells divide. They are termed 'high-grade' (or aggressive) when they divide quickly and 'indolent' (or low-grade) when they divide slowly. Mantle cell lymphoma exhibits a moderately aggressive course, it is rarely curable with currently available standard treatment. The registered annual incidence of non-Hodgkin's lymphoma in England and Wales is around 10,400 of these cases mantle cell lymphoma accounts for around 5 to 8%, equivalent to around 670 new diagnoses per year. Mantle cell lymphoma usually occurs in older adults (the median age of presentation is 60 years) and has a male predominance. Despite response rates of 50-70% with many regimens, mantle cell lymphoma typically progresses after chemotherapy. The median survival time is approximately 3 years; the 10-year survival rate is 5-10%.

Standard treatment options for the first-line treatment of mantle cell include; cyclophosphamide, doxorubicin, vincristine and prednisolone in combination with rituximab (R-CHOP) and fludarabine containing regimens.

The technology

Bendamustine (Levact, Napp Pharmaceuticals) is an alkylating antitumour agent. The antineoplastic and cytocidal effect of bendamustine hydrochloride is based on a cross-linking of DNA single and double strands by alkylation. As a result, DNA matrix functions and DNA synthesis and repair are impaired. It is administered by intravenous infusion.

Bendamustine in combination with rituximab does not currently have a UK marketing authorisation for the first-line treatment of mantle cell lymphoma. It has been studied in a clinical trial in comparison with R-CHOP for the first-line treatment of mantle cell lymphoma.

Intervention(s)	Bendamustine in combination with rituximab
Population(s)	People with previously untreated mantle cell lymphoma
Standard comparators	• cyclophosphamide, doxorubicin, vincristine and prednisolone plus rituximab (R-CHOP) • fludarabine containing regimens
Outcomes	The outcome measures to be considered include: • response rates • duration of response/remission • time to new anti-lymphoma treatment/time to progression • overall survival • progression free 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	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations	Related Technology Appraisals: Terminated Technology Appraisal No. 207, Oct 2010, 'Temsirolimus for the treatment of relapsed or refractory mantle cell lymphoma'. Related Cancer Service Guidelines: Cancer Service Guidelines, October 2003, 'Improving outcomes in haemato-oncology cancer'.

Questions for consultation

Have the most appropriate comparators for bendamustine in combination with rituximab for the first-line treatment of mantle cell lymphoma been included in the scope? Are the comparators listed routinely used in clinical practice? Is hyperfractionated cyclophosphamide, doxorubicin, vincristine, and dexamethasone (Hyper-CVAD) a relevant comparator? Is it used within the identified population?

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

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the scope may need changing in order to meet these aims.

In particular, please tell us if the scope:

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

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

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)