NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Bortezomib for previously untreated mantle cell lymphoma

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of bortezomib within its licensed indication for treating previously untreated mantle cell lymphoma.

Background

Lymphomas are cancers of the lymphatic system, which is a part of the immune system. Traditionally, lymphomas are divided into 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 and often aggressive type of non-Hodgkin's lymphoma which affects B-cells.

Approximately 10,800 people were diagnosed with non-Hodgkin's lymphoma in England in 2011, including approximately 500 with mantle cell lymphoma. Mantle cell lymphoma is more common in men than women (75% of people with mantle cell lymphoma are men), and it predominantly affects older people (the median age at presentation is 63 years). Most people with mantle cell lymphoma are diagnosed in advanced stages of the disease, with 80–90% of people diagnosed with Ann Arbor stage III or IV lymphoma.

Mantle cell lymphoma has been one of the most difficult types of non-Hodgkin's lymphoma to treat. Although it often responds well to initial chemotherapy, the duration of remission is often short and the median overall survival is 3–5 years. There is no accepted standard of care for mantle cell lymphoma, and the choice of treatment depends on the overall aim of therapy, the grade of disease, age and fitness.

There is currently no published NICE guidance on the treatment of mantle cell lymphoma. In clinical practice, most people with newly diagnosed mantle cell lymphoma are treated with chemotherapy. Chemotherapy options include combination regimens containing cyclophosphamide, fludarabine, vincristine, doxorubicin, cytarabine, chloramucil and/or bendamustine, often with rituximab; the most widely used regimens are rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP) and rituximab, fludarabine and cyclophosphamide (R-FC). If people are fit enough they may be treated with an intensive chemotherapy regimen, with a view to receiving a stem cell transplant once they are in remission. A small proportion of people with newly

diagnosed mantle cell lymphoma are managed with supportive or palliative care only.

The technology

Bortezomib (Velcade, Janssen) is an anticancer drug that works by reversible inhibition of multi-enzyme complexes known as proteasomes. By inhibiting proteasomes, bortezomib interferes with the cell cycle, leading to cell death. Bortezomib is administered by intravenous infusion.

Bortezomib does not currently have a UK marketing authorisation for treating mantle cell lymphoma. It is being studied in clinical trials as part of combination chemotherapy regimens, in adults with previously untreated mantle cell lymphoma. These studies include bortezomib in combination with rituximab, cyclophosphamide, doxorubicin and prednisone, compared with R-CHOP, in adults with previously untreated stage II, III or IV mantle cell lymphoma for whom bone marrow transplants are unsuitable.

Intervention(s)	Bortezomib in combination with rituximab, cyclophosphamide, doxorubicin and prednisone
Population(s)	People with previously untreated mantle cell lymphoma, for whom bone marrow transplants are unsuitable
Comparators	Established clinical management without bortezomib, including (but not limited to): • R-CHOP • R-CVP • R-FC • bendamustine plus rituximab • chlorambucil plus rituximab
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • overall response rate • duration of response/remission • time to new anti-lymphoma treatment/time to progression • 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 or CE marking. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 228, Jul 2011, 'Bortezomib and thalidomide for the first-line treatment of multiple myeloma'. Review Proposal Date Jul 2014. Technology Appraisal No. 129, Oct 2007, 'Bortezomib monotherapy for relapsed multiple myeloma'. Static list. Technology Appraisal in Preparation, 'Bortezomib for induction therapy prior to high dose chemotherapy and autologous stem cell transplantation for the treatment of multiple myeloma'. Earliest anticipated date of publication May 2014. Technology Appraisal in Preparation, 'Bendamustine in combination with rituximab for the first-line treatment of mantle cell lymphoma'. Publication TBC. Technology Appraisal in Preparation, 'Bortezomib for consolidation therapy after autologous stem cell transplantation for the treatment of multiple myeloma'. Publication TBC. Technology Appraisal in Preparation, 'Vorinostat in combination with bortezomib for the treatment of multiple myeloma in people who have received at least one prior therapy'. Publication TBC. Suspended Technology Appraisal, 'Bortezomib for the treatment of relapsed or refractory follicular non-Hodgkin's lymphoma'. Related Guidelines: Clinical Guideline in Preparation, 'Non-Hodgkin's

	lymphoma: diagnosis and management of non-Hodgkin's lymphoma'. Earliest anticipated date of publication Dec 2015. Cancer Service Guidance, Oct 2003, 'Improving outcomes in haemato-oncology cancer'. Related NICE Pathways: NICE Pathway: Blood and bone marrow cancers, Pathway created: Dec 2013. http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers/blood-and-bone-marrow-cancers-overview
Related National Policy	NHS Commissioning Board, Apr 2013, 'Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages)'. http://www.england.nhs.uk/wp-content/uploads/2013/10/b04-p-a.pdf Department of Health, Jan 2011, 'Improving Outcomes: A Strategy for Cancer'.

Questions for consultation

Should the appraisal be restricted to treating specific stages of mantle cell lymphoma?

Is bortezomib likely to be used in people for whom bone marrow transplants are appropriate?

Is bortezomib expected to only be used in combination with rituximab, cyclophosphamide, doxorubicin and prednisone, or is use in combination with other chemotherapy drugs likely? If the latter, which additional chemotherapy combinations should be included in this appraisal?

Have all relevant comparators for bortezomib been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for mantle cell lymphoma?
- Do all people with mantle cell lymphoma who are treated with chemotherapy also receive rituximab?

Have all the relevant outcomes been included in the scope?

- Would duration of remission or the time to progression or subsequent treatment be relevant outcome measures for people with mantle cell lymphoma treated with bortezomib?

Where do you consider bortezomib will fit into the existing NICE Pathway, Blood and bone marrow cancers?

Are there any subgroups of people in whom bortezomib 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 proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which bortezomib will be licensed;

- 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 bortezomib 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 bortezomib 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)