NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Bortezomib for previously untreated mantle cell lymphoma

Final scope

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. 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.

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, chlorambucil and/or bendamustine, often with rituximab; the most widely used regimens are rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP), rituximab, fludarabine and cyclophosphamide (R-FC) and rituximab and bendamustine. 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 and subcutaneous injection.

Bortezomib in combination with rituximab, cyclophosphamide, doxorubicin and prednisone has a UK marketing authorisation. It is indicated for the treatment of adult patients with previously untreated mantle cell lymphoma who are unsuitable for haematopoietic stem cell transplantation.

Intervention(s)	Bortezomib in combination with rituximab, cyclophosphamide, doxorubicin and prednisone
Population(s)	People with previously untreated mantle cell lymphoma, who are not going to have a stem cell transplant
Comparators	Established clinical management without bortezomib, including: • R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone) • bendamustine plus rituximab (with or without cytarabine) • R-FC (rituximab, fludarabine and cyclophosphamide)
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 in Preparation, 'Bendamustine in combination with rituximab for the first-line treatment of mantle cell lymphoma'. Publication TBC. Technology Appraisal in Preparation, 'Ibrutinib for the treatment of relapsed or refractory mantle cell lymphoma'. Publication TBC. 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	Department of Health, Jan 2011, 'Improving Outcomes: A Strategy for Cancer'.