NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ibrutinib for treating relapsed or refractory mantle cell lymphoma

Draft scope (pre-invitation)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ibrutinib within its marketing authorisation for treating relapsed or refractory 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 treatment for relapsed or refractory mantle cell lymphoma, and the choice of treatment depends on the overall aim of therapy, the grade of disease, age and fitness. The British Committee for Standards in Haematology (BCSH) guidelines recommend that treatment with rituximab (with or without cyclophosphamide and fludarabine), bortezomib, temsirolimus or combination chemotherapy should be considered. In NHS clinical practice, treatment for relapsed or refractory mantle cell lymphoma is most commonly rituximab combined with either bendamustine, or with cyclophosphamide, doxorubicin, vincristine and prednisolone. Temsirolimus is not used in clinical practice in England.

The technology

Ibrutinib (Imbruvica, Janssen) inhibits B-cell proliferation, and promotes cell death.

Ibrutinib has a marketing authorisation in the UK for the treatment of adult patients with relapsed or refractory mantle cell lymphoma. It is administered orally.

Intervention(s)	Ibrutinib
Population(s)	Adults with relapsed or refractory mantle cell lymphoma.
Comparators	Established clinical management without ibrutinib, including single agent and combination regimens with: • Bendamustine • Bendamustine and rituximab • Bendamustine, rituximab and cytarabine • Rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP) • Rituximab,cyclophosphamide, vincristine and prednisolone (R-CVP) • Fludarabine cyclophosphamide and rituximab (FCR)
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. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only 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: Appraisals in development 'Bortezomib for untreated mantle cell lymphoma' NICE technology appraisals guidance [ID724]. Publication expected Dec 2015. 'Bendamustine in combination with rituximab for the first-line treatment of mantle cell lymphoma' NICE technology appraisals guidance [ID609]. Suspended. Publication date to be confirmed. Related Guidelines: 'Improving outcomes in haemato-oncology cancers' Cancer Service Guidance, October 2003 Under review. Guidelines in development 'Non-Hodgkin's lymphoma: diagnosis and management of non-Hodgkin's lymphoma' Publication expected July 2016 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

Have all relevant comparators for ibrutinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for relapsed and refractory mantle cell lymphoma?

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 proposed scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which ibrutinib is 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 ibrutinib 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 ibrutinib 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.