NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Lenalidomide for treating relapsed or refractory mantle cell lymphoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of lenalidomide 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 body's immune system. Traditionally, lymphomas are divided into Hodgkin's lymphoma and non-Hodgkin lymphoma. Non-Hodgkin 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 lymphoma affecting the B-cells.

Approximately 10,800 people were diagnosed with non-Hodgkin 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 is one of the most difficult types of non-Hodgkin lymphoma to treat. Although it often responds well to initial chemotherapy, the duration of remission is often short. 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 and fitness of the person. The British Committee for Standards in Haematology (BCSH) guidelines recommend considering stem cell transplant (SCT) for those who are fit enough and have not received a SCT previously. For those not fit enough, a range of chemotherapy options are available. In NHS clinical practice, treatment for relapsed or refractory mantle cell lymphoma is most commonly rituximab combined with either bendamustine, with cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP), with fludarabine and cyclophosphamide (R-FC) or with cyclophosphamide, vincristine and prednisone (R-CVP). Other regimens containing bortezomib, chlorambucil, cytarabine, gemcitabine, ibrutinib or lenalidomide may also be used. Temsirolimus is not commonly used in NHS clinical practice. Bendamustine and ibrutinib have been used for treating relapsed or refractory mantle cell lymphoma in clinical practice through the Cancer Drugs Fund.

The technology

Lenalidomide (Revlimid, Celgene) is an immunomodulator and a structural analogue of thalidomide. It has anti-neoplastic, anti-angiogenic and pro-erythropoeitic properties. It is administered orally.

Lenalidomide does not currently have a marketing authorisation in the UK for relapsed or refractory mantle cell lymphoma. It is currently being studied in a clinical trial compared with the investigator's choice of single agent chemotherapy (chlorambucil, rituximab, cytarabine, gemcitabine, or fludarabine) in adults with relapsed or refractory mantle cell lymphoma.

Intervention(s)	Lenalidomide
Population(s)	People with relapsed or refractory mantle cell lymphoma
Comparators	Established clinical management without lenalidomide, including: Single agents such as: • Rituximab • Fludarabine • Chlorambucil • Cytarabine • Gemcitabine • Ibrutinib (subject to ongoing NICE appraisal) and combination regimens such as: • R-CHOP • R-FC • R-CVP • Bendamustine + rituximab • Chlorambucil + rituximab

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • overall response rates • 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. The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.
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: Technology Appraisal in Preparation 'Lymphoma (mantle cell, relapsed, refractory) – ibrutinib' NICE Technology Appraisal [ID753]. Earliest anticipated date of publication December 2016 Related Guidelines: Clinical Guideline in Preparation, 'Non-Hodgkin's lymphoma: diagnosis and management of non-Hodgkin's lymphoma'. Earliest anticipated date of publication July 2016. Cancer Service Guidance, Improving outcomes in

	haemato-oncology cancers, October 2003: http://www.nice.org.uk/nicemedia/live/10891/28786/28786.pdf 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, The NHS Outcomes Framework 2014/15, 2013 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf Department of Health, 'Improving Outcomes: A Strategy for Cancer' third annual report, Dec 2013 https://www.gov.uk/government/publications/the-national-cancer-strategy-3rd-annual-report--2 Department of Health, July 2011, 'Commissioning Cancer Services' https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/153603/dh_128690.pdf