NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Lenalidomide for treating relapsed or refractory mantle cell lymphoma

Draft scope (pre-referral)

Draft 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'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 affecting the 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 is 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 prednisone. Other regimens containing bortezomib, lenalidomide and cytarabine may also be used. Temsirolimus is not used. Although bendamustine and bortezomib have not been appraised by NICE for treating relapsed or refractory mantle cell lymphoma these treatments are used 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 agent and combination regimens with: • Rituximab • Cyclophosphamide • Doxorubicin • Vincristine • Bendamustine • Fludarabine • Chlorambucil • Cytarabine • Bortezomib • Ibrutinib • Prednisolone • Prednisone
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. Where comparator technologies are available through the Cancer Drugs Fund, the cost incurred by the Cancer Drug Fund should be used in any economic analyses, rather than the list price.
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 'Idelalisib for treating refractory indolent non-Hodgkin's lymphoma'. Suspended Proposed Technology Appraisal, 'Ibrutinib for treating relapsed or refractory mantle cell lymphoma'. Publication TBC Proposed Technology Appraisal, 'idelalisib in combination with rituximab for refractory indolent non-Hodgkin's 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, 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	NHS Commissioning Board, 'Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages)' Apr 2013 http://www.england.nhs.uk/wp-content/uploads/2013/10/b04-p-a.pdf 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

Questions for consultation

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

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

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

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 lenalidomide 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 lenalidomide 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 lenalidomide 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/article/pmg19/chapter/1-Introduction