NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ibrutinib for treating relapsed or refractory chronic lymphocytic leukaemia and small lymphocytic leukaemia

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ibrutinib within its licensed indication for treating relapsed or refractory chronic lymphocytic leukaemia and small lymphocytic leukaemia.

Background

Chronic lymphocytic leukaemia (CLL) is a malignant disorder of white blood cells (lymphocytes) which causes anaemia, swollen lymph nodes, spleen enlargement, weight loss and increased susceptibility to infection. CLL is an incurable disease which often remains undiagnosed until it is well advanced. CLL and small lymphocytic lymphoma (SLL) are considered as being the same condition. In CLL, cancer cells are found mostly in the blood and bone marrow. In SLL, cancer cells are found mostly in the lymph nodes.

CLL is the most common form of leukaemia and there are an estimated 2300 new diagnoses in England each year. The risk of developing CLL increases with age and is more common in men. The 5-year survival rates for all stages of CLL are 44% and 52% for men and women respectively.

Treatment options vary depending on factors such as stage of CLL, performance status and co-morbidities. For previously untreated CLL, NICE technology appraisal guidance 174 recommends fludarabine, cyclophosphamide and rituximab (FCR) combination therapy as an option for treating first-line CLL in people for whom fludarabine in combination with cyclophosphamide is considered appropriate. NICE technology appraisal guidance 216 recommends bendamustine as an option for the first-line treatment of CLL (Binet stage B or C) in people for whom fludarabine combination chemotherapy is not appropriate.

NICE technology appraisal guidance 193 recommends FCR as an option for people with relapsed or refractory CLL unless their disease is refractory to fludarabine or has been previously treated with rituximab. Bendamustine is commonly used off-label in clinical practice and is available through the Cancer Drugs Fund with or without rituximab in people with relapsed CLL for whom FCR is unsuitable. Chlorambucil is also used with or without rituximab in people with relapsed CLL for whom FCR is unsuitable. NICE does not recommend ofatumumab for treating CLL refractory to fludarabine and alemtuzumab (NICE technology appraisal guidance 202), but it is available through the Cancer Drugs Fund.

The technology

Ibrutinib (Imbruvica, Janssen) is an oral inhibitor of a protein called Bruton's Tyrosine Kinase, which stops B-cell (lymphocyte) proliferation and promotes cell death.

Ibrutinib does not currently have a UK marketing authorisation for treating relapsed or refractory CLL and SLL. It has been studied in clinical trials compared with ofatumumab in adults with relapsed or refractory CLL or SLL who have received at least one prior therapy and for whom a purine analogue based therapy was not suitable.

Intervention(s)	Ibrutinib
Population(s)	People with relapsed or refractory chronic lymphocytic leukaemia or small lymphocytic leukaemia, for whom cutotoxic therapies are not suitable
Comparators	• Bendamustine (with or without rituximab) • Chlorambucil (with or without rituximab) • Best supportive care
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rates • 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. 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 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	Technology Appraisal No. 202, October 2010, 'Ofatumumab for the treatment of chronic lymphocytic leukaemia refractory to fludarabine and alemtuzumab'. Review deferred until publication of ongoing clinical trials. Technology Appraisal No. 193, July 2010, 'Rituximab for the treatment of relapsed chronic lymphocytic leukamia'. Review proposal currently being considered. Related Guidelines: NICE cancer service guidance (2003). Improving outcomes in haematological cancers. Related NICE Pathways: NICE pathway on blood and bone marrow cancers, available at: http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers
Related National Policy	National service framework: 'Improving outcomes: a strategy for cancer', Jan 2011. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/135516/dh_123394.pdf.pdf

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 or refractory chronic lymphocytic leukaemia and small lymphocytic leukaemia?
- Should ofatumumab be considered as a comparator?
- How should best supportive care be defined?

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

Where do you consider ibrutinib will fit into the existing NICE pathway for '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 ibrutinib 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 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.

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)