NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ibrutinib for untreated chronic lymphocytic leukaemia

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ibrutinib within its marketing authorisation for untreated chronic lymphocytic leukaemia.

Background

Chronic lymphocytic leukaemia (CLL) is a malignant disorder of white blood cells (lymphocytes). It causes anaemia, swollen lymph nodes, spleen enlargement, weight loss and increased susceptibility to infection.

In England around 3,000 people were diagnosed with CLL in 2013.[1] The risk of developing CLL increases with age and it is more common in men. Median survival ranges from about 3 to over 10 years depending on the genetic subtype and the stage at which the disease is diagnosed.[2]

Treatment options vary depending on factors such as stage of CLL, performance status and co-morbidities. For people with untreated chronic lymphocytic leukaemia, fludarabine combination therapy is the standard of care when immediate treatment is needed. NICE technology appraisal guidance 193 recommends rituximab only in combination with fludarabine and cyclophosphamide. Fludarabine combination therapy may not be suitable for about half the people needing immediate treatment, for example, people who have comorbidities such as impaired renal function, hypertension or diabetes. NICE technology appraisal 216 recommends bendamustine as a first-line treatment of chronic lymphocytic leukaemia for people who cannot have fludarabine. Obinutuzumab in combination with chlorambucil (NICE Technology appraisal 343), or ofatumumab in combination with chlorambucil (NICE Technology appraisal 344) are recommended as treatment options when bendamustine-based therapy is not suitable. In clinical practice treatment options also include chlorambucil with or without rituximab.

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 has been studied in clinical trials compared with chlorambucil in people with one or more comorbidities that may preclude them from treatment with fludarabine, cyclophosphamide and rituximab. Ibrutinib does not have a marketing authorisation in the UK for this population.

Ibrutinib has a marketing authorisation in the UK for treating adult patients with CLL 'who have received at least one prior therapy, or in first line in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo-immunotherapy'.

Intervention(s)	Ibrutinib
Population(s)	People with untreated chronic lymphocytic leukaemia for whom fludarabine combination chemotherapy is unsuitable
Comparators	People for whom bendamustine-based therapy is suitable: • bendamustine, with or without rituximab People for whom bendamustine-based therapy is unsuitable: • chlorambucil, with or without rituximab • obinutuzumab with chlorambucil • ofatumumab with chlorambucil
Outcomes	The outcome measures to be considered include: • overall survival • progression-free 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. The availability of any patient access schemes for the intervention or comparator technologies will 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: 'Obinutuzumab in combination with chlorambucil for untreated chronic lymphocytic leukaemia (2015). NICE Technology Appraisal 343. Review date June 2018. 'Ofatumumab in combination with chlorambucil or bendamustine for untreated chronic lymphocytic leukaemia' (2015). NICE Technology Appraisal 344. Review date June 2018. 'Ofatumumab for the treatment of chronic lymphocytic leukaemia refractory to fludarabine and alemtuzumab' (2010). NICE Technology Appraisal 202. Review Proposal Date to be confirmed. 'Rituximab for the treatment of relapsed chronic lymphocytic leukamia' (2010). NICE Technology Appraisal 193. Moved to the static list, March 2014. Appraisals in development: 'Ibrutinib for treating chronic lymphocytic leukaemia' NICE technology appraisals guidance [ID749]. Publication to be confirmed. 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 NHS England Manual for prescribed specialised services 2013/2014. Specialist cancer services (adults) [section 105, page 234]:

	http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf NHS England 2013/14 NHS standard contract for cancer: chemotherapy (adult). Section B part 1- service specifications: http://www.england.nhs.uk/wp-content/uploads/2013/06/b15-cancr-chemoth.pdf Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1–5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.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 untreated CLL for whom fludarabine is not suitable?
- Is rituximab monotherapy part of established clinical practice in the NHS for CLL for whom fludarabine is not suitable?

Are the outcomes listed appropriate?

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, 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/article/pmg19/chapter/1-Introduction)

References

1. Office for National Statistics (2015). Cancer registration statistics. Accessed November 2015.

2. Cancer Research UK (2015). Statistics and outlook for chronic lymphocytic leukaemia. Accessed November 2015.