NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Idelalisib in combination with ofatumumab for previously treated chronic lymphocytic leukaemia [ID817]

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of idelalisib in combination with ofatumumab within its marketing authorisation for previously treated 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. CLL is the most common form of leukaemia.

CLL is the most common form of leukaemia and there are an estimated 2300 new diagnoses in England each year. Approximately 75% of people with CLL are diagnosed when they are over the age of 60. The risk of developing CLL increases with age and is more common in men. Median survival ranges from about 3 to 12 years depending on the genetic subtype and the stage at which the disease is diagnosed.

Treatment options vary depending on factors such as stage of CLL, performance status and co-morbidities. NICE technology appraisal guidance 193 recommends fludaribine, cyclophosphamide and rituximab (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 outside its marketing authorisation in clinical practice in England with or without rituximab through the Cancer Drugs Fund. Chlorambucil has a UK marketing authorisation for CLL and is used in clinical practice in England with or without rituximab in people with relapsed or refractory CLL for whom FCR is unsuitable. NICE does not recommend ofatumumab for treating CLL refractory to fludarabine (NICE technology appraisal guidance 202). NICE has not published guidance for idelalisib in combination with rituximab for previously treated CLL (NICE technology appraisal in preparation ID764), but it is used in clinical practice in England through the Cancer Drugs Fund. NICE has not published guidance for ibrutinib for previously treated CLL (NICE technology appraisal in preparation ID749), but it is used in clinical practice in England through the Cancer Drugs Fund.

The technology

Idelalisib (Zydelig, Gilead Sciences) is an oral inhibitor of serine-threonine protein kinase enzymes that regulate key cellular functions including proliferation, cell death and migration.

Idelalisib in combination with ofatumumab does not have a marketing authorisation in the UK. It has been studied in clinical trials compared with ofatumumab alone in adults with previously treated chronic lymphocytic leukaemia.

Idelalisib has a marketing authorisation in the UK in combination with rituximab "for the treatment of adult patients with chronic lymphocytic leukaemia who have received at least one prior therapy or, as first-line treatment in the presence of 17p deletion or TP53 mutation in patients unsuitable for chemo-immunotherapy.

Intervention(s)	Idelalisib in combination with ofatumumab
Population(s)	People with previously treated chronic lymphocytic leukaemia
Comparators	• bendamustine (not licensed in the UK for this indication, funded via the CDF) with or without rituximab • chlorambucil with or without rituximab • fludarabine in combination with cyclophosphamide and rituximab • ibrutinib (NICE guidance is in development, funded by the CDF in the interim) • idelalisib in combination with rituximab (NICE guidance is in development, funded by the CDF in the interim) • best supportive care (including but not limited to, regular monitoring, blood transfusions, infection control and psychological support).

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. Where comparator technologies are available through the Cancer Drug Fund, the cost incurred by the Cancer Drug Fund should be used in any economic analyses, rather than the list price. If appropriate, the appraisal should include consideration of the costs and implications of additional testing for genetic markers, but will not make recommendations on specific diagnostic tests or devices.
Other considerations	If the evidence allows, the following subgroup will be considered: • presence or absence of 17p deletion. 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	Technology Appraisal No. 202, October 2010, 'Ofatumumab for the treatment of chronic lymphocytic leukaemia refractory to fludarabine and alemtuzumab'. Review Proposal Date TBC. Technology Appraisal No. 193, July 2010, 'Rituximab for the treatment of relapsed chronic lymphocytic leukaemia'. Review Proposal Date January 2014.

	ID764, Technology Appraisal in Preparation, 'Idelalisib for treating chronic lymphocytic leukaemia'. Earliest anticipated date of publication October 2015. ID749, Technology Appraisal in Preparation, 'Ibrutinib for treating chronic lymphocytic leukaemia'. Earliest anticipated date of publication December 2015. 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	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 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 idelalisib in combination with ofatumumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for previously treated chronic lymphocytic leukaemia?

For which population(s) with previously treated chronic lymphocytic leukaemia would high-dose corticosteroids with or without rituximab be considered suitable? Should it be included as a comparator for this proposed appraisal?

'How should best supportive care be defined?'

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom idelalisib in combination with ofatumumab is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider idelalisib in combination with ofatumumab 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 idelalisib in combination with ofatumumab 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 idelalisib in combination with ofatumumab 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 idelalisib in combination with ofatumumab 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)