NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Idelalisib for treating chronic lymphocytic leukaemia

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of idelalisib within its licensed indication for 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.

In England around 2,700 people were diagnosed with CLL in 2010. 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.

Approximately 5% to 10% of people diagnosed with CLL are considered to have 'high-risk' disease characterised by the presence of cytogenetic mutation or abnormalities (that is, 17p deletion or TP53 mutation). The presence of 17p deletion or TP53 mutation influences the rate of cell growth as well as the resistance of the disease to treatment. People with high risk disease with the 17p deletion or TP53 mutation have a median survival of 2 to 3 years.

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), but it is used in clinical practice in England.

In people with symptomatic disease who have untreated chronic lymphocytic leukaemia, FCR combination therapy is the preferred treatment option, while chlorambucil or bendamustine are commonly used in patients for whom FCR is unsuitable. NICE technology appraisal guidance 174 recommends the use

of rituximab in combination with fludarabine and cyclophosphamide as a first-line treatment option for people who are able to take fludarabine and cyclophosphamide, and does not recommend rituximab in combination with other chemotherapies. NICE technology appraisal guidance TA119 does not recommend fludarabine monotherapy as a first-line treatment for people with CLL. NICE technology appraisal guidance 216 recommends bendamustine as an option for the first-line treatment of CLL (Binet stage B or C) in patients for whom fludarabine combination chemotherapy is not appropriate. Ofatumumab in combination with bendamustine or chlorambucil and obinutuzumab in combination with chlorambucil are subject to ongoing NICE technology appraisals. In clinical practice in England, patients with untreated CLL associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable are treated with bendamustine (with or without rituximab), chlorambucil (with or without rituximab) or alemtuzumab. Alemtuzumab does not have a marketing authorisation for CLLin the European Union; alemtuzumab was withdrawn in this indication at the request of the company manufacturing it for commercial reasons. However it is currently available in England through a patient access programme agreed by the company and the European Medicines Agency.

The technology

Idelalisib (Zydelig, Gilead Sciences) is an oral inhibitor of enzymes that regulate key cellular functions including proliferation, cell death and migration. 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 rituximab
Population(s)	• Adults with chronic lymphocytic leukaemia who have received at least one therapy • Adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation for whom chemo-immunotherapy is not suitable

Comparators	For adults with chronic lymphocytic leukaemia who have received at least one prior therapy: • Fludarabine in combination with cyclophosphamide and rituximab • Bendamustine (with or without rituximab) • Chlorambucil (with or without rituximab) • Corticosteroids (with or without rituximab) • Ofatumumab • Best supportive care (including but not limited to, regular monitoring, blood transfusions, infection control and psychological support). For adults with untreated chronic lymphocytic leukaemia associated with 17p deletion or TP53 mutation • Bendamustine (with or without rituximab) • Chlorambucil (with or without rituximab) • Alemtuzumab • Best supportive care (including but not limited to regular monitoring, blood transfusions, infection control and psychological support) • Ofatumumab in combination with bendamustine or chlorambucil (subject to ongoing NICE technology appraisal) • Obinutuzumab in combination with chlorambucil (subject to ongoing NICE technology appraisal)
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. 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. Where comparator technologies are available through the Cancer Drugs Fund, the cost incurred by the Cancer Drugs Fund should be used in economic analyses.
Other considerations	If the evidence allows, the following subgroup will be considered for adults with chronic lymphocytic leukaemia who have received at least one prior therapy: • Presence or absence of 17p deletion. 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	Related Technology Appraisals: 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 leukamia'. Guidance on static list. Technology appraisal No. 216, February 2011, Bendamustine for the first-line treatment of chronic lymphocytic leukaemia. Transferred to the static list, February 2014. Technology appraisal No.174, June 2009, Rituximab for first-line treatment of chronic lymphocytic leukaemia. Transferred to the static list, March 2014. Technology appraisal No.119, February 2007, Fludarabine monotherapy for the first-line treatment

	ofchronic lymphocytic leukaemia. Transferred to the static list, May 2010. Technology Appraisal in Preparation, 'Obinutuzumab in combination with chlorambucil for untreated chronic lymphocytic leukaemia ' Earliest anticipated date of publication February 2015 Technology Appraisal in Preparation, 'Ofatumumab in combination with chlorambucil or bendamustine for untreated chronic lymphocytic leukaemia'.Earliest anticipated date of publication April 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	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 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