NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Obinutuzumab in combination with chlorambucil for previously untreated chronic lymphocytic leukaemia

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of obinutuzumab within its licensed indication for previously untreated chronic lymphocytic leukaemia.

Background

Chronic lymphocytic leukaemia (CLL) is a malignant disorder of white blood cells (lymphocytes). CLL 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. 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. In people with symptomatic disease, fludarabine, cyclophosphamide and rituximab (FCR) combination therapy is the preferred treatment option in previously untreated patients, while chlorambucil or bendamustine is commonly used in patients for whom FCR is unsuitable. NICE guidance (TA174) 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 guidance (TA119) does not recommend fludarabine monotherapy as a first-line treatment for people with CLL. NICE guidance (TA216) 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.

The technology

Obinutuzumab (Gazyva, Roche Products) is a type 2 glycoengineered antibody that binds to the CD20 protein present on B cells, except stem or plasma cells, and causes cell death. It is administered by intravenous infusion.

Obinutuzumab does not currently have a UK marketing authorisation for previously untreated CLL. It has been studied in a clinical trial that compared obinutuzumab in combination with chlorambucil, rituximab in combination with

chlorambucil, and chlorambucil alone. The trial recruited adults with CLL who had not previously received treatment and had impaired renal function or other comorbidities. In this trial, the dose of chlorambucil was lower than the dose typically used in the UK.

Intervention(s)	Obinutuzumab with chlorambucil
Population	People with previously untreated chronic lymphocytic leukaemia for whom fludarabine combination chemotherapy is unsuitable
Comparators	• Chlorambucil, with or without rituximab • Bendamustine, with or without rituximab
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • minimal residual disease negativity • 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations	Related Technology Appraisals: Technology appraisal No. 216, Feb 2011, Bendamustine for the first-line treatment of chronic lymphocytic leukaemia. Transferred to the static list, February 2014. Technology appraisal No.174, Jun 2009, Rituximab for first-line treatment of chronic lymphocytic leukaemia. Review proposal in progress, Mar 2014. Technology appraisal No.119, Feb 2007, Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia. Transferred to the static list, May 2010. Technology Appraisal in Preparation, Ofatumumab in combination with chlorambucil or bendamustine for previously untreated chronic lymphocytic leukaemia. Earliest anticipated date of publication Apr 2015. Related Clinical Guidelines: NICE cancer service guidance (2003). Improving outcomes in haematological 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 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