NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Obinutuzumab for previously untreated chronic lymphocytic leukaemia

Draft scope (pre-referral)

Draft 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 disorder of white blood cells (lymphocytes) which causes anaemia and increased susceptibility to infection. CLL is a malignant disease (that is, it progressively worsens and potentially results in death). It is chronic, incurable and often remains undiagnosed until it is well advanced.

CLL is the most common form of leukaemia and approximately 2,400 people are diagnosed in the UK each year. CLL mainly affects older people and 75% of people with CLL are diagnosed when they are over the age of 60. CLL has several genetic subtypes. The median survival ranges from about 3 to 12 years, depending on the genetic subtype and the stage at which the disease is diagnosed.

The treatment options for CLL vary depending on factors such as the stage of CLL, performance status and co-morbidities. The majority of people with CLL are asymptomatic when they present, and many never need treatment. Approximately 67% of patient will need treatment. For people with symptomatic disease who are in good health fludarabine, cyclophosphamide and rituximab combination therapy (FCR) is commonly used as a first line treatment. NICE technology appraisal 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. For those who are not considered well enough for FCR other treatment options include chlorambucil (with or without rituximab), bendamustine (with or without rituximab) or dose reduced FCR. NICE technology appraisal 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. NICE technology appraisal 119 does not recommend fludarabine monotherapy as a first-line treatment for people with CLL.

The technology

Obinutuzumab (brand name unknown, Roche Products) is an antibody that binds to the CD20 protein present on all 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 combination with chlorambucil in a clinical trial in adults with CLL who had not previously received treatment compared with rituximab in combination with chlorambucil, and chlorambucil alone.

Intervention(s)	Obinutuzumab with chlorambucil
Population	People with previously untreated chronic lymphocytic leukaemia
Comparators	• Fludarabine and cyclophosphamide (with or without rituximab) In people for whom fludarabine combination therapy is not appropriate: • 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 • 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 and NICE pathways	Related Technology Appraisals: Technology appraisal No. 216, February 2011, Bendamustine for the first-line treatment of chronic lymphocytic leukaemia. Review proposal date December 2013. Technology appraisal No.174, June 2009, Rituximab for first-line treatment of chronic lymphocytic leukaemia. Review proposal date 2013. Technology appraisal No.119, February 2007, Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia. Static list. Related Clinical Guidelines: NICE cancer service guidance (2003). Improving outcomes in haematological cancers.
Related NHS England policy	None

Questions for consultation

Have all relevant comparators for obinutuzumab been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for previously untreated chronic lymphocytic leukaemia?
- Is fludarabine always used in combination with both cyclophosphamide and rituximab in clinical practice?
- Should fludarabine in combination with cyclophosphamide, and fludarabine in combination with rituximab also be listed as comparators?
- Is alemtuzumab still commonly used for treating previously untreated chronic lymphocytic leukaemia and therefore a relevant comparator for this appraisal?
- Should dose reduced fludarabine, cyclophosphamide and rituximab combination therapy be listed as a comparator, for people who are not able to have fludarabine combination therapy?

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

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 obinutuzumab 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 the technology 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 the technology 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).

Subject to referral by the Department of Health, the invite for participation for this technology appraisal is anticipated for after January 2014, when new arrangements for the pricing of pharmaceuticals are expected to be in place. Consequences for this appraisal will be explored through further consultation on the scope pre-invitation.