Scope:

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Ofatumumab for the maintenance treatment of relapsed chronic lymphocytic leukaemia

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ofatumumab within its licensed indication for the maintenance treatment of relapsed chronic lymphocytic leukaemia.

Background

Chronic lymphocytic leukaemia (CLL) is a malignant disorder of white blood cells (lymphocytes). CLL causes abnormal lymphocytes to proliferate, which in turn causes anaemia and increased susceptibility to infection. CLL often remains undiagnosed either until it is well advanced, or until a chance test shows abnormally high levels of lymphocytes in the blood. It is a chronic and incurable disease. CLL is the most common form of leukaemia in the UK.

In the UK, there are around 2800 cases of CLL diagnosed each year. It mainly affects older people, with 75% of diagnoses in people over the age of 60. Overall incidence is approximately 4 per 100,000 per year. CLL is genetically heterogeneous with median survival ranging from 3 to 12 years depending on the genetic subtype and the stage at which the disease is diagnosed. Other prognostic factors include age of onset, spread of disease and response to treatment.

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 some never need treatment. Approximately 67% of patients will need treatment. For people with symptomatic CLL, NICE technology appraisal 174 recommends initial treatment with fludarabine, cyclophosphamide and rituximab combination therapy (FCR). For people for whom fludarabine combination chemotherapy is not appropriate, chlorambucil (with or without rituximab) or bendamustine (with or without rituximab; NICE technology appraisal 216) may be considered. Fludarabine monotherapy is not recommended by NICE as an initial treatment option for CLL (NICE technology appraisal 119).

For people with relapsed disease, treatments used previously may be administered again either with or without the addition of another therapeutic

agent, or alternatively a different agent may be used. People may be offered a stem cell transplant. NICE technology appraisal 193 recommends rituximab in combination with fludarabine and cyclophosphamide as a treatment option for people with relapsed or refractory CLL providing the condition has previously responded to fludarabine and the patient has not previously been treated with rituximab (unless in the context of a clinical trial at a lower dose than the licenced dose for CLL, or in combination with chemotherapy other than fludarabine and cyclophosphamide). There are currently no licensed maintenance treatment regimens used in England for CLL if the disease has not progressed immediately following chemotherapy. Watchful waiting is the current standard of care after chemotherapy. The frequency of surveillance should be dependent on risk of recurrence, as judged by the multi-disciplinary team involved in patient care.

The technology

Ofatumumab (Arzerra; GSK) is a humanised monoclonal antibody targeted against the CD20 cell surface antigen of B-cell membranes. Ofatumumab is administered by intravenous infusion.

Ofatumumab does not currently have a UK marketing authorisation for the maintenance treatment of relapsed CLL. It is being studied in a clinical trial compared with no maintenance treatment (observation) in adults with relapsed chronic lymphocytic leukaemia whose disease has subsequently responded to second or third line treatment.

Ofatumumab currently has a UK marketing authorisation for people with CLL whose disease has not responded to treatment with fludarabine and alemtuzumab. NICE technology appraisal guidance 202 does not recommend ofatumumab for this indication.

Intervention(s)	Ofatumumab maintenance treatment
Population(s)	People with relapsed chronic lymphocytic leukaemia
Comparators	Established clinical practice without ofatumumab maintenance treatment (including surveillance)

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 and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 216, Dec 2013, 'Bendamustine for the treatment of chronic lymphocytic leukaemia'. Review proposal currently being considered. Technology Appraisal No. 202, Oct 2010, 'Ofatumumab for the treatment of chronic lymphocytic leukaemia refractory to fludarabine and alemtuzumab'. Review deferred until publication of ongoing clinical trials. Technology Appraisal No. 193, Jul 2010, 'Rituximab for the treatment of relapsed or refractory chronic lymphocytic leukaemia'. Review proposal currently being considered. Technology Appraisal No. 174, Jul 2009, 'Rituximab for the first line treatment of chronic lymphocytic leukaemia'. Review proposal currently being considered. Technology Appraisal No. 119, Feb 2007, 'Fludarabine monotherapy for the first-line treatment of chronic lymphocytic leukaemia'. Guidance on the static list. Related Guidelines: Cancer Service Guidelines, Oct 2003. Improving outcomes in haematological cancers. Related NICE pathway: Blood and bone marrow cancers. Created Dec 2013. Available at: http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers
Related National Policy	Manual for prescribed specialist services chapter 105. Specialist cancer services (adults) http://www.england.nhs.uk/wp-content/uploads/2012/12/pss-manual.pdf

Questions for consultation

Ofatumumab has been studied in clinical trials as a maintenance treatment for people with relapsed CLL whose disease has subsequently responded to second or third line treatment. Have all relevant comparators for ofatumumab maintenance treatment (used in line with the clinical trials) been included in the scope? Which treatments, if any, are considered to be established clinical practice in the NHS for maintenance treatment of CLL?

Are there any subgroups of people in whom ofatumumab 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 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.

Where will ofatumumab maintenance treatment fit in the existing NICE pathway for 'Blood and bone marrow cancers'?

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)