NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Elotuzumab for previously treated multiple myeloma [ID855]

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of elotuzumab within its marketing authorisation for previously treated multiple myeloma.

Background

Multiple myeloma is a form of cancer that arises from plasma cells (a type of white blood cell) in the bone marrow. Myeloma cells produce large quantities of an abnormal antibody, known as paraprotein. Unlike normal antibodies, paraprotein has no useful function and lacks the ability to fight infection. Myeloma cells supress the development of normal blood cells that are responsible for fighting infection (white blood cells), carrying oxygen around the body (red blood cells) and blood clotting (platelets). The term multiple myeloma refers to the presence of more than one site of affected bone at the time of diagnosis. People with multiple myeloma can experience bone pain, bone fractures, tiredness (due to anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems.

In 2011, 4039 people were diagnosed with multiple myeloma in England[1]. Forty three percent of people diagnosed are aged 75 years and over[1]. Multiple myeloma is more common in men than in women and the incidence is also reported to be higher in people of African family origin[1]. The 5-year survival rate for adults with multiple myeloma in England is estimated to be 37%[1].

Multiple myeloma is an incurable disease. The main aims of therapy are to prolong survival and maintain quality of life by controlling the disease and relieving symptoms. Following initial treatment, subsequent therapy is influenced by previous treatment and response to it, duration of remission, comorbidities and patient preference. NICE technology appraisal guidance 129 recommends bortezomib monotherapy as an option for treating progressive multiple myeloma in people who are at first relapse having received 1 prior therapy and who have undergone, or are unsuitable for bone marrow transplantation. NICE technology appraisal guidance 171 recommends lenalidomide in combination with dexamethasone as a treatment option for people with multiple myeloma who have received at least 2 prior therapies, and is under part-review by NICE for people with multiple myeloma who have received 1 prior treatment with bortezomib. However, lenalidomide is available through the Cancer Drugs Fund for people with multiple myeloma who have received 1 prior therapy. NICE technology appraisal guidance 338 does not recommend pomalidomide in combination with low-dose

dexamethasone for relapsed and refractory multiple myeloma, but it is available through the Cancer Drugs Fund. Bendamustine does not have a marketing authorisation in the UK for treating relapsed and refractory multiple myeloma, but it is available through the Cancer Drugs Fund for relapsed myeloma when other treatments are contraindicated or inappropriate. Other subsequent treatment options may include repeating high-dose chemotherapy or chemotherapy with alkylating agents and anthracyclines, thalidomide and corticosteroids.

The technology

Elotuzumab (brand name unknown, Bristol-Myers Squibb) is an intravenous humanised recombinant monoclonal antibody that kills multiple myeloma cells.

Elotuzumab does not currently have a marketing authorisation in the UK for previously treated multiple myeloma. It has been studied in clinical trials in combination with lenalidomide plus dexamethasone, and in combination with bortezomib plus dexamethasone, in people with multiple myeloma previously treated with 1 to 3 therapies, compared with lenalidomide plus dexamethasone alone, and bortezomib plus dexamethasone alone, respectively.

Intervention(s)	• elotuzumab in combination with lenalidomide and dexamethasone • elotuzumab in combination with bortezomib and dexamethasone
Population(s)	People with multiple myeloma who have received at least 1 therapy

Comparators	After 1 therapy: • bortezomib monotherapy • bortezomib in combination with dexamethasone • lenalidomide in combination with dexamethasone (NICE guidance is in development, funded by the CDF in the interim) After 2 or more therapies: • bortezomib in combination with dexamethasone • lenalidomide in combination with dexamethasone • bendamustine (not appraised by NICE but funded via the CDF) • pomalidomide in combination with low-dose dexamethasone (not recommended by NICE but funded via the CDF) • chemotherapy including regimens based on mephalan, vincristine, cyclophosphamide and doxorubicin
Outcomes	The outcome measures to be considered include: • progression-free survival • overall 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. The availability of any patient access schemes for the intervention or comparator technologies should be taken into account. 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.
Other considerations	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. If the evidence allows, subgroup analyses based on number of lines of previous therapy will be considered.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 129, October 2007, 'Bortezomib monotherapy for relapsed multiple myeloma'. Guidance on Static list. Technology Appraisal No. 171, June 2009, 'Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy'. Guidance on Static list. Technology Appraisal No. 338, March 2015, 'Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib'. Review proposal date March 2018. ID663, Technology Appraisal in Preparation, 'Panobinostat for treating multiple myeloma in people who have received at least one prior therapy'. Earliest anticipated date of publication January 2016. ID667, Suspended Technology Appraisal, 'Lenalidomide for the treatment of multiple myeloma in people who

	have received at least one prior therapy with bortezomib (partial review of NICE technology appraisal guidance 171)'. Related Guidelines: Clinical Guideline in Preparation, 'Myeloma: diagnosis and management of myeloma'. Earliest anticipated date of publication January 2016. Cancer Service Guidance, October 2003, 'Improving Outcomes in Haematological Cancer'. Related NICE Pathways: NICE pathway: Blood and bone marrow cancers, pathway last updated 24 February 2015 http://pathways.nice.org.uk/blood-and-bone-marrow-cancers
Related National Policy	NHS England Manual for prescribed specialised services 2013/2014. Blood and marrow transplantation services (all ages) [section 29, page 78–79]: 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, 4–5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf

Questions for consultation

Have all relevant comparators for elotuzumab been included in the scope? Which treatments are considered to be established clinical practice in the NHS for previously treated multiple myeloma?

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

Where do you consider elotuzumab 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 elotuzumab 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 elotuzumab 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 elotuzumab 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)

References

1. Cancer Research UK (2013). Multiple myeloma incidence statistics. Accessed April 2015.