NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Elotuzumab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of elotuzumab in combination with pomalidomide and low-dose dexamethasone within its marketing authorisation for treating relapsed and refractory 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 capacity 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 2015, 4,632 people were diagnosed with multiple myeloma in England.[1] It is most frequently diagnosed in older people, with 44% of new cases in England in people aged 75 years and over.[2] 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.[3] The 5-year survival rate for adults with multiple myeloma in England and Wales is about 47%.[4]

The main aims of therapy are to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. For people whose disease is relapsed or refractory after at least 1 prior therapy:

- NICE technology appraisal guidance 457 recommends carfilzomib in combination with dexamethasone as a treatment option for people that had only 1 previous therapy which did not include bortezomib.

- NICE technology appraisal guidance 129 recommends bortezomib monotherapy as an option for people who are at first relapse having had 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 who have received 2 or more prior therapies.

- NICE technology appraisal guidance 380 recommends panobinostat in combination with bortezomib and dexamethasone as a treatment option for people who have received at least 2 prior therapies including bortezomib and an immunomodulatory agent.

- NICE technology appraisal guidance 427 recommends pomalidomide in combination with low-dose dexamethasone as a treatment option after 3 previous treatments including both lenalidomide and bortezomib.

- NICE technology appraisal guidance 505 recommends ixazomib citrate in combination with lenalidomide and dexamethasone for use within the Cancer Drugs Fund after 2 or 3 previous therapies

- NICE technology appraisal guidance 510 recommends daratumumab monotherapy for use within the Cancer Drugs Find after 3 previous therapies

The technology

Elotuzumab (Empliciti, Bristol Myers-Squibb) is an immunostimulatory humanised, IgG1 monoclonal antibody that specifically targets the signalling lymphocyte activation family member 7 (SLAMF7) protein. Activating this protein stimulates the body's immune cells to kill myeloma cells. It is administered intravenously.

Elotuzumab does not currently have a marketing authorisation in the UK in combination with pomalidomide and dexamethasone. Elotuzumab in combination with pomalidomide and dexamethasone has been studied in a randomised controlled trial compared with pomalidomide and dexamethasone. People in the trial had refractory and relapsed and refractory multiple myeloma and had had 2 or more previous treatments including lenalidomide and a proteasome inhibitor alone or in combination. Elotuzumab has a marketing authorisation in combination with lenalidomide and dexamethasone for the treatment of multiple myeloma in adults who have received at least one prior therapy.

The marketing authorisation for pomalidomide (Immovid, Celgene) is for the treatment of adults with relapsed and refractory multiple myeloma who have received at least 2 prior regimens including both lenalidomide and bortezomib.

Intervention(s)	Elotuzumab in combination with pomalidomide and dexamethasone

Population(s)	People with relapsed or refractory multiple myeloma who have received 2 or more previous treatments including lenalidomide and a proteasome inhibitor.
Comparators	For people who have had 2 prior therapies: • Panobinostat in combination with bortezomib and dexamethasone For people who have had 3 or more prior therapies: • Pomalidomide in combination with dexamethasone • Panobinostat in combination with bortezomib and dexamethasone
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 will be taken into account.
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.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (2018) NICE technology appraisal guidance 510

	Multiple myeloma (relapsed, refractory) - ixazomib citrate. (2018) NICE technology appraisal guidance 505 Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (2017) NICE technology appraisal guidance 427 Panobinostat for treating multiple myeloma after at least 2 previous treatments (2016) NICE technology appraisal guidance 380 Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy (2009) NICE technology appraisal guidance 171 **Terminated appraisals** Bortezomib for treating multiple myeloma after second or subsequent relapse (terminated appraisal). (2017) NICE technology appraisal guidance 453. Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal). (2017) NICE technology appraisal guidance 454 Elotuzumab for previously treated multiple myeloma (terminated appraisal). (2017) NICE technology appraisal guidance 434 **Appraisals in development (including suspended appraisals)** Daratumumab with bortezomib for treating relapsed or refractory multiple myeloma. NICE technology appraisal guidance [ID974]. Publication expected October 2018 Pomalidomide in combination with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma. NICE appraisal guidance [ID1358]. Publication date to be confirmed Plitidepsin in combination with dexamethasone for treating relapsed or refractory multiple myeloma. NICE technology appraisal guidance [ID1081]. Suspended. Pembrolizumab for previously treated multiple myeloma.

	NICE technology appraisal guidance [ID1139]. Suspended. Multiple myeloma (one prior therapy) - vorinostat (with bortezomib). NICE technology appraisal guidance [ID501]. Publication date to be confirmed. Suspended Multiple myeloma - lenalidomide (post bortezomib) (part rev TA171). NICE technology appraisal guidance [ID667]. Publication date to be confirmed. Suspended Multiple myeloma - bortezomib (consolidation therapy). NICE technology appraisal guidance [ID529]. Publication date to be confirmed. Suspended Lenalidomide in combination with dexamethasone for previously untreated multiple myeloma. NICE technology appraisal guidance [ID667] Elotuzumab for untreated multiple myeloma. NICE technology appraisal guidance [ID966]. Publication date to be confirmed Lenalidomide with bortezomib and dexamethasone for untreated multiple myeloma. NICE technology appraisal guidance [ID1449]. Publication date to be confirmed **Related Guidelines:** Haematological cancers: improving outcomes (2016) NICE guideline 47 Myeloma: diagnosis and management (2016) NICE guideline 35 **Related Quality Standards:** Haematological cancers (2017) NICE quality standard 150 **Related NICE Pathways:** Myeloma (2017) NICE pathway
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Blood and marrow transplantation services (adults and children) [section 29, page 79] Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1,4,5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 Department of Health (2016) NHS outcomes framework 2016 to 2017

	Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy

Questions for consultation

At which point in the treatment pathway would elotuzumab with pomalidomide and dexamethasone be used in current clinical practice?
Have all relevant comparators for elotuzumab with pomalidomide and dexamethasone been included in the scope?

Are the outcomes listed appropriate?

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

Where do you consider elotuzumab with pomalidomide and dexamethasone will fit into the existing NICE pathway, Myeloma?

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 with pomalidomide and dexamethasone 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 with pomalidomide and dexamethasone 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 with pomalidomide and dexamethasone 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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 'Myeloma incidence by sex and UK region'. Accessed July 2018.
[2] Office of national statistics 'Cancer registration statistics, England'. Accessed July 2018.
[3] National cancer institute 'SEER Cancer Statistics Review, 1975-2008'. Accessed July 2018.
[4]Cancer Research UK 'Myeloma survival'. Accessed July 2018.

