NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Isatuximab with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of isatuximab in combination with pomalidomide and dexamethasone within its marketing authorisation for treating relapsed or 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 suppress 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]

Multiple myeloma is an incurable disease. Therapy aims to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. If the disease progresses after initial treatment, the choice of subsequent therapy is influenced by previous treatment and response to it, duration of remission, comorbidities and patient preference.

For people whose disease is relapsed or refractory after 2 prior therapies:

- 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 Fund after 3 previous therapies.

Isatuximab in combination with pomalidomide and dexamethasone is being studied in adults who have previously received at least two prior multiple myeloma treatment regimens which included lenalidomide and a proteasome inhibitor. There are 2 on-going (currently suspended) appraisals for lenalidomide, one in newly diagnosed multiple myeloma and the other after one prior therapy. The positioning of isatuximab in combination with pomalidomide and dexamethasone in the treatment pathway may therefore be impacted by the output of these appraisals.

The technology

Isatuximab is a humanised monoclonal antibody which binds to cell surface glycoprotein CD38. This may trigger antitumor antibody-dependent cellular cytotoxicity (ADCC), complement-dependent cytotoxicity (CDC), inhibition of enzymatic activity and apoptosis eventually leading to cell lysis in CD38-expressing tumour cells. Isatuximab is administered intravenously.

Isatuximab (brand name unknown, Sanofi) does not currently have a marketing authorisation in the UK. It is being studied in clinical trials in combination with pomalidomide and dexamethasone compared with pomalidomide and dexamethasone alone, for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least 2 lines of prior therapies which included lenalidomide and a proteasome inhibitor, and whose disease progressed on the last therapy.

Intervention(s)	Isatuximab in combination with pomalidomide and dexamethasone
Population(s)	Adults with relapsed or refractory multiple myeloma who have received at least 2 or more previous treatments, including lenalidomide and a proteasome inhibitor.

Comparators	For people who have had 2 previous 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:** 'Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma.' (2018) NICE technology appraisal guidance 505. Review date expected December 2019. 'Daratumumab monotherapy for treating relapsed and refractory multiple myeloma.' (2018) NICE technology

	appraisal guidance 510. Review date expected November 2020. 'Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib.' (2017) NICE technology appraisal guidance 427. Review date expected January 2020. 'Panobinostat for treating multiple myeloma after at least 2 previous treatments.' (2016). NICE Technology Appraisal 380. Review date expected January 2019. 'Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy.' (2009). NICE Technology Appraisal 171. Guidance on static list 2014. **Terminated appraisals:** 'Elotuzumab for treating relapsed or refractory multiple myeloma' NICE technology appraisal guidance [ID855]. (terminated appraisal). **Appraisals in development (including suspended appraisals):** 'Pomalidomide in combination with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma' [ID1358] (suspended appraisal). 'Elotuzumab with pomalidomide and dexamethasone for treating multiple myeloma after 2 therapies' [ID1467] (suspended appraisal). 'Plitidepsin in combination with dexamethasone for treating relapsed or refractory multiple myeloma' [ID1081] (suspended appraisal). 'Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy' Partial review of NICE technology appraisal guidance 171 [ID667] (suspended appraisal). 'Lenalidomide in combination with dexamethasone for previously untreated multiple myeloma' [ID474] (suspended appraisal). **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

Have all relevant comparators for isatuximab in combination with pomalidomide and dexamethasone been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for multiple myeloma?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom isatuximab in combination 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 isatuximab in combination 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 isatuximab in combination 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 isatuximab in combination 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 isatuximab in combination 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

[1] Cancer Research UK. Available from: 'Myeloma incidence by sex and UK region'. Accessed 5th December 2018.

[2] Office of national statistics. Available from: 'Cancer registration statistics, England'. Accessed 5th December 2018.

[3] National cancer institute. Available from: 'SEER Cancer Statistics Review, 1975-2008'. Accessed 5th December 2018.

[4]Cancer Research UK Available from: 'Myeloma survival'. Accessed 5th December 2018.

