NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of selinexor with bortezomib and low-dose dexamethasone within its marketing authorisation for treating relapsed 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 suppress the development of normal blood cells that are responsible for fighting infection, carrying oxygen around the body and blood clotting. 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, infections, hypercalcaemia (too much calcium in the blood) and kidney problems.

In 2017, 5,034 people were diagnosed with multiple myeloma in England.[1] It is most frequently diagnosed in older people, with 43% 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.[1, 2] The 5-year survival rate for adults with multiple myeloma in England and Wales is about 52%.[3]

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 at least 1 prior therapy:

- NICE technology appraisal guidance 129 recommends bortezomib monotherapy as an option for treating progressive multiple myeloma in people who are at first relapse and who have undergone, or are unsuitable for, bone marrow transplantation.

- NICE technology appraisal guidance 457 recommends carfilzomib plus dexamethasone as a treatment option for adults who had only 1 previous therapy which did not include bortezomib.

- NICE technology appraisal guidance 586 recommends lenalidomide plus dexamethasone as a treatment option for adults who had only 1 previous therapy which included bortezomib.

- NICE technology appraisal guidance 573 recommends daratumumab plus bortezomib and dexamethasone for use within the Cancer Drugs Fund as a treatment option for adults who have had 1 previous therapy.

For people who have had at least 2 prior therapies:

- NICE technology appraisal guidance 171 recommends lenalidomide plus dexamethasone as a treatment option for people who have had at least 2 previous therapies.

- NICE technology appraisal guidance 380 recommends panobinostat plus bortezomib and dexamethasone as a treatment option for adults who have had at least 2 previous therapies including bortezomib and an immunomodulatory agent.

- NICE technology appraisal guidance 505 recommends ixazomib citrate plus lenalidomide and dexamethasone for use within the Cancer Drugs Fund as a treatment option for adults who have had 2 or 3 previous therapies.

For people who have had at least 3 prior therapies:

- NICE technology appraisal guidance 427 recommends pomalidomide plus low-dose dexamethasone as a treatment option for adults who have had at least 3 previous treatments including both lenalidomide and bortezomib.

- NICE technology appraisal guidance 510 recommends daratumumab monotherapy for use within the Cancer Drugs Fund as a treatment option for adults who have had 3 previous therapies including a proteasome inhibitor and an immunomodulator.

The technology

Selinexor (KPT-330, Karyopharm Therapeutics) is a selective inhibitor of nuclear export, which works by blocking the protein called exportin 1 (XPO1). Preventing the action of XPO1 proteins enhances anti-cancer proteins and induces death of cancerous cells. It is administered orally.

Selinexor does not currently have a marketing authorisation in the UK for treating multiple myeloma. It has been studied in combination with bortezomib and low-dose dexamethasone in an open-label, randomised clinical trial in adults with multiple myeloma who have had between 1 and 3 prior therapies.

Intervention(s)	Selinexor in combination with bortezomib and low-dose dexamethasone
Population(s)	People with relapsed refractory multiple myeloma who have had 1 to 3 prior lines of therapy
Comparators	For people who have had 1 previous therapy: • bortezomib • carfilzomib plus dexamethasone • lenalidomide plus dexamethasone For people who have had 2 previous therapies: • isatuximab plus pomalidomide and dexamethasone (subject to ongoing NICE appraisal) • lenalidomide plus dexamethasone • panobinostat plus bortezomib and dexamethasone For people who have had 3 or more previous therapies: • isatuximab plus pomalidomide and dexamethasone (subject to ongoing NICE appraisal) • lenalidomide plus dexamethasone • panobinostat plus bortezomib and dexamethasone • pomalidomide plus dexamethasone For people who have received any number of previous therapies: • conventional chemotherapy regimens (for example, melphalan and cyclophosphamide) • best supportive care
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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out. 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 commercial arrangements for the intervention, comparator and subsequent treatment 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:** Lenalidomide plus dexamethasone for multiple myeloma after 1 treatment with bortezomib. (2019) NICE technology appraisal guidance 586. Review date expected 2022. Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma. (2019) NICE technology appraisal guidance 573. Review date expected 2021. Daratumumab monotherapy for treating relapsed and refractory multiple myeloma. (2018) NICE technology appraisal guidance 510. Review date expected November 2020. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma. (2018) NICE technology appraisal guidance 505. Review date expected December 2019. Carfilzomib for previously treated multiple myeloma. (2017) NICE technology appraisal guidance 457.

	Review date expected July 2020. Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (2017) NICE technology appraisal guidance 427. Review date expected 2020. Panobinostat for treating multiple myeloma after at least 2 previous treatments. (2016) NICE technology appraisal guidance 380. Reviewed January 2019, nothing new was found that affects the recommendations. Lenalidomide for the treatment of multiple myeloma in people who have received at least 2 prior therapies. (2009). NICE technology appraisal guidance 171. Guidance on static list 2014. Bortezomib monotherapy for relapsed multiple myeloma. (2007) NICE technology appraisal guidance 129. Guidance on static list 2012. **Terminated appraisals** Pomalidomide with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2019) NICE technology appraisal guidance 602. 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. Elotuzumab for treating relapsed or refractory multiple myeloma NICE technology appraisal guidance [ID855]. (terminated appraisal). Multiple myeloma - carfilzomib (with lenalidomide and dexamethasone, after prior therapy) [ID677] NICE technology appraisal guidance. (terminated appraisal). **Appraisals in development (including suspended appraisals)** Isatuximab with carfilzomib and dexamethasone for treating relapsed or refractory multiple myeloma

	[ID1620]. Publication expected August 2020. Isatuximab with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma [ID1477] Publication expected August 2020. Ixazomib with lenalidomide and dexamethasone for untreated multiple myeloma [ID1170] Publication expected August 2020. Selinexor with low-dose dexamethasone for treating refractory multiple myeloma [ID1535]. Publication expected January 2021. Carfilzomib with dexamethasone and lenalidomide for treating multiple myeloma after at least 1 previous therapy [ID1493]. Publication date to be confirmed. Elotuzumab for multiple myeloma [ID966]. NICE technology appraisals guidance. Publication date to be confirmed. Elotuzumab with pomalidomide and dexamethasone for treating multiple myeloma after 2 therapies [ID1467]. [Suspended]. Multiple myeloma (one prior therapy) - vorinostat (with bortezomib) [ID501]. [Suspended]. Pembrolizumab for previously treated multiple myeloma [ID1139]. [Suspended]. Plitidepsin in combination with dexamethasone for treating relapsed or refractory multiple myeloma [ID1081]. [Suspended]. Pomalidomide in combination with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma [ID1358] [Suspended]. **Related Guidelines:** Myeloma: diagnosis and management (2016). NICE guideline 35. Review date February 2019. Haematological cancers – improving outcomes (2016) NICE guideline 47 Review date to be confirmed. **Related Quality Standards:** Haematological cancers (2017) NICE quality standard 150 **Related NICE Pathways:** Myeloma (2017) NICE pathway
Related National	The NHS Long Term Plan, 2019. NHS Long Term Plan

Policy	NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 29: blood and marrow transplantation services (adults and children) p98 NHS England (Jan 2015) National chemotherapy algorithms - multiple myeloma Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1 and 2.

Questions for consultation

Have all relevant comparators for selinexor with bortezomib and low-dose dexamethasone been included in the scope?

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

How should best supportive care be defined?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom selinexor with bortezomib and low-dose dexamethasone is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider selinexor with bortezomib and low-dose 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 selinexor with bortezomib and low-dose 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 selinexor with bortezomib and low-dose 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 selinexor with bortezomib and low-dose 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. Office of national statistics 'Cancer registration statistics, England'. Accessed July 2020.

2. National cancer institute 'SEER Cancer Statistics Review, 1975-2016'. Accessed February 2020.

3. Cancer Research UK 'Myeloma survival'. Accessed July 2020.