NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

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

Final scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of selinexor with 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, 4,799 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 origin. [1, 2] The 5-year survival rate for adults with multiple myeloma in England and Wales is about 47%.[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 low-dose dexamethasone in a single-arm clinical trial in adults with multiple myeloma who:

- have had 3 or more prior therapeutic regimens including: an alkylating agent, lenalidomide, pomalidomide, bortezomib, carfilzomib, daratumumab and a glucocorticoid, and

- are refractory to previous treatment with one or more glucocorticoid, a proteasome inhibitor (bortezomib and or carfilzomib), an immunomodulatory agent (lenalidomide and or pomalidomide) and an anti-CD38 monoclonal antibody (daratumumab).

A pre-specified subgroup of the study contained participants described as "penta-refractory", who had previously received bortezomib, carfilzomib, lenalidomide, pomalidomide and daratumumab, as well as alkylating agents, and whose disease was refractory to at least 3 of these. This group had had a median of 7 previous therapies.

Intervention	Selinexor with low-dose dexamethasone
Population	People with relapsed refractory multiple myeloma who have had at least 3 prior lines of therapy.
Comparators	• Pomalidomide in combination with low-dose dexamethasone • Panobinostat in combination with bortezomib and dexamethasone • 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. 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. If evidence allows, the following subgroup analyses will be considered: • cytogenetic risk factors • prior lines of therapy, including patients who have had at least three prior lines of therapy and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent and one anti-CD38 monoclonal antibody.
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. 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) Selinexor with low-dose dexamethasone for treating refractory multiple myeloma [ID1535]. Publication expected January 2021. Ixazomib with lenalidomide and dexamethasone for untreated multiple myeloma [ID1170] Publication expected August 2020. 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. 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 Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan 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.

References

1. Office of national statistics 'Cancer registration statistics, England'. Accessed February 2020.

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

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