**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Evaluation**

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

**Final scope**

## Final remit/evaluation objective

To appraise the clinical and cost effectiveness of selinexor with bortezomib and low-dose 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 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.

Approximately 5,000 people are diagnosed with multiple myeloma in England each year (2016 to 2018 data).[1] Five-year prevalence of multiple myeloma in the UK is estimated to be 26 per 100,000.[2] It is most frequently diagnosed in older people, with about 43% of new cases of multiple myeloma in England in people aged 75 years or older.[1] The 10-year survival rate for people with multiple myeloma in England is estimated to be 29%.[3] The incidence rates are reported to be lower in the Asian ethnic group, higher in the Black ethnic group, and similar in people of mixed or multiple ethnicity, compared with the White ethnic group, in England (2013-2017 data).[3]

The main aims of therapy are to prolong survival and maintain a good quality of life by controlling the condition and relieving symptoms. If the condition 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 condition is relapsed or refractory after at least 1 prior therapy, NICE recommends:

- bortezomib monotherapy for people who are at first relapse and who have undergone, or are unsuitable for, bone marrow transplantation (technology appraisal guidance 129), although this is rarely used in clinical practice.
- lenalidomide plus dexamethasone (technology appraisal guidance 586) and carfilzomib plus lenalidomide and dexamethasone (technology appraisal guidance 695) for people who had bortezomib.

- carfilzomib plus dexamethasone for people who have not had bortezomib (technology appraisal guidance 657).
- daratumumab plus bortezomib and dexamethasone for people who previously had lenalidomide or when lenalidomide is unsuitable as a second-line treatment (technology appraisal guidance 897).

For people whose condition is relapsed or refractory after at least 2 prior therapies, NICE recommends:

- lenalidomide plus dexamethasone (technology appraisal guidance 171).
- ixazomib plus lenalidomide and dexamethasone (technology appraisal guidance 870).
- panobinostat plus bortezomib and dexamethasone for people who had bortezomib and an immunomodulatory agent (technology appraisal guidance 380).

For people whose condition is relapsed or refractory after at least 3 prior therapies, NICE recommends:

- pomalidomide plus low-dose dexamethasone for people who had both lenalidomide and bortezomib (technology appraisal guidance 427).
- daratumumab monotherapy for people who had a proteasome inhibitor and an immunomodulator (technology appraisal guidance 783).
- isatuximab plus pomalidomide and dexamethasone for use within the Cancer Drugs Fund for people who had both lenalidomide and a proteasome inhibitor (technology appraisal guidance 658).

**The technology**

Selinexor (Nexpovio, Menarini-Stemline UK) is indicated in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have had at least 1 prior therapy.

It also has a marketing authorisation in the UK, in combination with dexamethasone, for the treatment of adult patients with multiple myeloma who have had at least 4 prior therapies and whose disease is refractory to at least 2 proteasome inhibitors, 2 immunomodulatory agents and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

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| **Intervention(s)** | Selinexor in combination with bortezomib and dexamethasone |
| **Population(s)** | People with relapsing or refractory multiple myeloma who have had 1 to 3 prior therapies |

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| **Subgroups** | If the evidence allows the following subgroups will be considered:<br>• prior therapies |
| **Comparators** | For people who have had 1 prior therapy:<br>• bortezomib monotherapy<br>• lenalidomide plus dexamethasone<br>• carfilzomib plus lenalidomide and dexamethasone<br>• carfilzomib plus dexamethasone<br>• daratumumab plus bortezomib and dexamethasone<br>For people who have had 2 prior therapies:<br>• lenalidomide plus dexamethasone<br>• ixazomib plus lenalidomide and dexamethasone<br>• panobinostat plus bortezomib and dexamethasone<br>For people who have had 3 or more prior therapies:<br>• pomalidomide plus low-dose dexamethasone<br>• daratumumab monotherapy<br>• ixazomib plus lenalidomide and dexamethasone<br>• lenalidomide plus dexamethasone<br>• panobinostat plus bortezomib and dexamethasone<br>• isatuximab plus pomalidomide and dexamethasone (subject to ongoing NICE appraisal)<br>For people who have had any number of prior therapies:<br>• conventional chemotherapy regimens<br>• best supportive care<br>• belantamab mafodotin (subject to ongoing NICE appraisal) |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rates<br>• adverse effects of treatment<br>• health-related quality of life. |

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| **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.<br><br>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.<br><br>Costs will be considered from an NHS and Personal Social Services perspective.<br><br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.<br><br>The availability and cost of biosimilar and generic products should 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** | **Related technology appraisals**<br><br>Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma (2023) NICE technology appraisal guidance 897.<br><br>Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (2023) NICE technology appraisal guidance 870.<br><br>Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (2022) NICE technology appraisal guidance 783.<br><br>Carfilzomib with dexamethasone and lenalidomide for previously treated multiple myeloma (2021) NICE technology appraisal guidance 695.<br><br>Carfilzomib for previously treated multiple myeloma (2020) NICE technology appraisal guidance 657.<br><br>Lenalidomide plus dexamethasone for multiple myeloma after 1 treatment with bortezomib (2019) NICE technology appraisal guidance 586.<br><br>Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomibv (2017) NICE technology appraisal guidance 427.<br><br>Panobinostat for treating multiple myeloma after at least 2 previous treatments (2016) NICE technology appraisal guidance 380. |

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| | Lenalidomide for the treatment of multiple myeloma in people who have received at least 2 prior therapies (2009) NICE technology appraisal guidance 171.<br><br>Bortezomib monotherapy for relapsed multiple myeloma (2007) NICE technology appraisal guidance 129.<br><br>**Related technology appraisals in development**<br><br>Belantamab mafodotin for treating relapsed or refractory multiple myeloma after 3 therapies. NICE technology appraisal guidance [ID2701] Publication expected August 2023.<br><br>Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma (review of TA658). NICE technology appraisal guidance [ID4067] Publication expected December 2023.<br><br>**Related NICE guidelines**<br><br>Myeloma: diagnosis and management (2018) NICE guideline NG35.<br><br>Haematological cancers: improving outcomes (2016) NICE guidance 47.<br><br>**Related Quality Standards**<br><br>Haematological cancers (2017) NICE quality standard 150. |
| **Related National Policy** | The NHS Long Term Plan, 2019. NHS Long Term Plan<br><br>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019)<br><br>NHS England (2020) Bendamustine for relapsed multiple myeloma (all ages). Clinical Commissioning Policy. Reference: 200604P |

**References**

1. Office for National Statistics (2019) Cancer registration statistics, England. Accessed June 2023.

2. World Health Organisation International Agency for Research on Cancer (2021) United Kingdom fact sheet. Accessed June 2023.

3. Cancer Research UK. Myeloma statistics. Accessed June 2023.