NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Selinexor with dexamethasone for treating relapsed or refractory multiple myeloma [ID6193]

Final scope

Final remit/evaluation objective

To appraise the clinical and cost effectiveness of selinexor with 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, tiredness (due to anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems.[1]

Approximately 5,000 people are diagnosed with multiple myeloma in England each year (2016 to 2018 data)[2]. Five-year prevalence of multiple myeloma in the UK is estimated to be 26 per 100,000.[3] 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.[4] The 10-year survival rate for people with multiple myeloma in England is estimated to be 29%.[5] 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).[5]

The main aims of therapy are 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 treatment, 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 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 treatments, NICE recommends:

- lenalidomide plus dexamethasone (technology appraisal guidance 171) .

- ixazomib citrate plus lenalidomide and dexamethasone (technology appraisal guidance 870).

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

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

- pomalidomide plus low-dose dexamethasone for people who have had both lenalidomide and bortezomib (technology appraisal guidance 427).

- daratumumab monotherapy for people who have 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) has a marketing authorisation in the UK in combination with dexamethasone for treating multiple myeloma in adult patients 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. It also has a marketing authorisation in the UK in combination with bortezomib and dexamethasone for the treatment of adult patients with multiple myeloma who have had at least 1 prior therapy.

Intervention(s)	Selinexor with dexamethasone
Population(s)	People with relapsed or refractory multiple myeloma who have had 4 or more treatments and whose disease is refractory to at least 2 proteasome inhibitors, 2 immunomodulatory agents and an anti-CD38 monoclonal antibody (penta-refractory), and who have demonstrated disease progression on the last therapy.

Subgroups	If evidence allows, the following subgroups will be considered: • cytogenetic risk factors
Comparators	• Pomalidomide in combination with low-dose dexamethasone • Panobinostat in combination with bortezomib and dexamethasone • Belantamab mafodotin (subject to ongoing NICE appraisal) • Conventional chemotherapy regimens • 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. 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:**

	Bortezomib and thalidomide for the first-line treatment of multiple myeloma (2011) NICE technology appraisal guidance 228. Bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation (2014) NICE technology appraisal guidance 311. Lenalidomide plus dexamethasone for multiple myeloma after 1 treatment with bortezomib. (2019) NICE technology appraisal guidance 586. Lenalidomide plus dexamethasone for previously untreated multiple myeloma (2019) NICE technology appraisal guidance 587. Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma (review of TA573). (2023) NICE technology appraisal guidance 897. Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma (2020) NICE technology appraisal guidance 658. Lenalidomide maintenance treatment after an autologous stem cell transplant for newly diagnosed multiple myeloma (2021) NICE technology appraisal guidance 680. Carfilzomib with dexamethasone and lenalidomide for previously treated multiple myeloma (2021) NICE technology appraisal guidance 695. Daratumumab in combination for untreated multiple myeloma when a stem cell transplant is suitable (2022) NICE technology appraisal guidance 763. Daratumumab monotherapy for treating relapsed and refractory multiple myeloma. (2018) NICE technology appraisal guidance 783. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma. (2018) NICE technology appraisal guidance 870. Carfilzomib for previously treated multiple myeloma. (2017) NICE technology appraisal guidance 657. 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 2 prior therapies. (2009, updated 2019). NICE technology appraisal guidance 171.

	Bortezomib monotherapy for relapsed multiple myeloma. (2007) NICE technology appraisal guidance 129. **Related technology appraisals in development:** Belantamab mafodotin for treating relapsed or refractory multiple myeloma after 4 or more therapies. NICE technology appraisal guidance [ID2701] Publication expected August 2023 Ciltacabtagene autoleucel for treating relapsed or refractory multiple myeloma. NICE technology appraisal guidance [ID3816] Publication date to be confirmed Elranatamab for treating relapsed or refractory multiple myeloma after 3 therapies. NICE technology appraisal guidance [ID4026] Publication expected February 2024 Idecabtagene vicleucel for treating relapsed and refractory multiple myeloma in people who have received at least 3 prior therapies. NICE technology appraisal guidance [ID1442] Publication date to be confirmed Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma (review of TA658). NICE technology appraisal guidance [ID4067] Publication expected December 2023 Ixazomib citrate for maintenance treatment of untreated multiple myeloma in people who cannot have autologous stem cell transplant. NICE technology appraisal guidance [ID2706] Publication date to be confirmed Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma. NICE technology appraisal guidance [ID3797] Publication date to be confirmed Teclistamab for treating relapsed or refractory multiple myeloma after 3 therapies. NICE technology appraisal guidance [ID5087] Publication date to be confirmed Venetoclax with dexamethasone for treating relapsed or refractory t(11;14)-positive multiple myeloma after lenalidomide and a proteasome inhibitor. NICE technology appraisal guidance [ID4040] Publication date to be confirmed **Related NICE guidelines:** Myeloma: diagnosis and management (2016). NICE guideline 35.

	Haematological cancers – improving outcomes (2016) NICE guideline 47. **Related quality standards:** Haematological cancers (2017) NICE quality standard 150
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2020) Bendamustine for relapsed multiple myeloma (all ages). Clinical Commissioning Policy. Reference 200604P 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. Myeloma UK (2021) What is myeloma?
2. Cancer Research UK, Myeloma incidence statistics
3. World Health Organisation International Agency for Research on Cancer (2021) United Kingdom fact sheet.
4. National Cancer Institute 'SEER Cancer Statistics Review, 1975-2016'
5. Cancer Research UK. Myeloma statistics.