

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Pomalidomide with dexamethasone for treating relapsed and refractory multiple myeloma after at least two regimens including lenalidomide and bortezomib (review of TA338)

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pomalidomide within its marketing authorisation for treating relapsed and refractory multiple myeloma previously treated with both lenalidomide and bortezomib.

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 2013, 4,703 people were diagnosed with multiple myeloma in England¹. Forty-three percent of people diagnosed are aged 75 years and over¹. Multiple myeloma is more common in men than in women and the incidence is also reported to be higher in people of African family origin¹. The 5-year survival rate for adults with multiple myeloma in England is estimated to be 47%². The main aims of therapy are to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms.

For initial treatment:

- NICE technology appraisal guidance 311 recommends bortezomib as an option, in combination with dexamethasone or with dexamethasone and thalidomide, for the induction treatment of adults with untreated multiple myeloma who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation.
- When stem-cell transplantation is not suitable, NICE technology appraisal guidance 228 recommends thalidomide or bortezomib (only if the person is unable to tolerate or has contraindications to thalidomide)

as an option, in combination with an alkylating agent (melphalan or cyclophosphamide) and a corticosteroid (prednisolone or dexamethasone).

Following 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.
- An ongoing NICE technology appraisal is assessing lenalidomide for treating multiple myeloma after 1 prior treatment with bortezomib.

For people who have had at least 2 prior therapies:

- NICE technology appraisal guidance 171 recommends lenalidomide in combination with dexamethasone as a treatment option.
- NICE technology appraisal guidance 380 recommends panobinostat in combination with bortezomib and dexamethasone as a treatment option for people with relapsed and refractory multiple myeloma who have received at least 2 prior therapies including bortezomib and an immunomodulatory agent.

For people who have had at least 3 prior therapies, treatment options include bendamustine (available through the Cancer Drugs Fund) or conventional chemotherapy regimens (for example, alkylating agents such as melphalan and cyclophosphamide).

NICE technology appraisal guidance 338 does not recommend pomalidomide within its marketing authorisation for treating relapsed and refractory multiple myeloma. NICE has decided to review technology appraisal 338 because:

- new clinical evidence is available
- the company is proposing a patient access scheme for pomalidomide.

The technology

Pomalidomide (Imnovid, Celgene) is an oral immunomodulatory drug analogue of thalidomide that directly inhibits myeloma growth.

Pomalidomide in combination with dexamethasone has a marketing authorisation in the UK for 'the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least 2 prior treatment

regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on last therapy’.

Intervention(s)	Pomalidomide in combination with dexamethasone
Population(s)	Adults with relapsed and refractory multiple myeloma who have had at least 2 prior treatment regimens, including both lenalidomide and bortezomib, and whose disease progressed on the last therapy
Comparators	<p>For people who have had 2 prior therapies:</p> <ul style="list-style-type: none"> • panobinostat in combination with bortezomib and dexamethasone <p>For people who have had 3 or more prior therapies:</p> <ul style="list-style-type: none"> • panobinostat in combination with bortezomib and dexamethasone • bendamustine (not appraised by NICE but funded via the Cancer Drugs Fund; does not currently have a marketing authorisation in the UK for this indication) • conventional chemotherapy regimens (for example, melphalan and cyclophosphamide)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rates • adverse effects of treatment • health-related quality of life.

<p>Economic analysis</p>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.</p>
<p>Other considerations</p>	<p>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.</p> <p>When appropriate, validation of the economic model may use comparators included in the clinical trial that are not listed in the 'Comparators' section above.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>'Panobinostat for treating multiple myeloma after at least 2 previous treatments' (2016). NICE Technology Appraisal 380. Review date January 2019.</p> <p>'Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib' (2015). NICE Technology Appraisal 338.</p> <p>'Bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation' (2014). NICE Technology Appraisal 311. Review date February 2017.</p> <p>'Bortezomib and thalidomide for the first-line treatment of multiple myeloma' (2011). NICE Technology Appraisal 228. Guidance on static list.</p> <p>'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.</p> <p>'Bortezomib monotherapy for relapsed multiple myeloma' (2007). NICE Technology Appraisal 129.</p>

	<p>Guidance on Static list.</p> <p>Appraisals in development:</p> <p>'Carfilzomib for previously treated multiple myeloma' NICE technology appraisal [ID934]. Publication date April 2017.</p> <p>'Ixazomib citrate in combination with lenalidomide and dexamethasone for relapsed or refractory multiple myeloma' NICE technology appraisal [ID807]. Publication date January 2017.</p> <p>'Lenalidomide for treating multiple myeloma after 1 prior treatment with bortezomib (part-review of TA171)' NICE technology appraisal [ID667]. Publication date to be confirmed.</p> <p>Clinical guidelines:</p> <p>'Myeloma: diagnosis and management of myeloma' (2016). NICE guideline 35.</p> <p>Related NICE Pathways:</p> <p>NICE pathway: Myeloma (2016)</p> <p>http://pathways.nice.org.uk/pathways/myeloma</p>
<p>Related National Policy</p>	<p>NHS England (2015) 'Cancer Drugs Fund list v6.1'</p> <p>NHS England Manual for prescribed specialised services 2013/2014. Blood and marrow transplantation services (all ages) [section 29, page 78–79]:</p> <p>http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf</p> <p>Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1, 4–5.</p> <p>https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf</p>

References

1. Cancer Research UK (2013). Multiple myeloma incidence statistics. Accessed February 2016.
2. Cancer Research UK (2011). Multiple myeloma survival statistics. Accessed February 2016.