

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Appraisal

### Daratumumab in combination with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma

#### Final scope

##### Final remit/appraisal objective

To appraise the clinical and cost effectiveness of daratumumab in combination with bortezomib and 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, bone fractures, tiredness (due to anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems.

In 2014, 5,501 people were diagnosed with multiple myeloma in England.<sup>1</sup> Of people diagnosed in the UK, 59% are aged 70 years and over. 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.<sup>2</sup> The 5-year survival rate for adults with multiple myeloma in England and Wales is about 47%.<sup>3</sup>

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 with relapsed or refractory disease after at least 1 previous treatment:

- NICE technology appraisal guidance 129 recommends bortezomib monotherapy as an option for people who are at first relapse having had 1 prior therapy and who have undergone, or are unsuitable for bone marrow transplantation.

- NICE technology appraisal guidance 457 recommends carfilzomib in combination with dexamethasone as an option for treating multiple myeloma in adults, only if they have had only 1 previous therapy, which did not include bortezomib
- NICE technology appraisal guidance 171 recommends lenalidomide in combination with dexamethasone as an option for the treatment of multiple myeloma in people who have received 2 or more prior therapies.
- 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.
- NICE technology appraisal guidance 427 recommends pomalidomide in combination with dexamethasone for treating multiple myeloma in adults at third or subsequent relapse

### The technology

Daratumumab (Darzalex, Janssen-Cilag) is a humanised monoclonal antibody that kills multiple myeloma cells, targeting the CD38 protein. It is administered intravenously.

Daratumumab in combination with bortezomib and dexamethasone has a marketing authorisation in the UK for the treatment of adult patients with multiple myeloma who have received at least 1 prior therapy.

<b>Intervention(s)</b>	Daratumumab in combination with bortezomib and dexamethasone
<b>Population(s)</b>	Adults with relapsed or refractory multiple myeloma who have had at least 1 previous treatment.
<b>Comparators</b>	<p>For people who have had 1 previous therapy, depending on previous therapy:</p> <ul style="list-style-type: none"> <li>• Bortezomib-based therapy</li> <li>• Carfilzomib in combination with dexamethasone</li> <li>• Combination chemotherapy</li> </ul> <p>For people who have had 2 previous therapies:</p> <ul style="list-style-type: none"> <li>• Lenalidomide in combination with dexamethasone</li> <li>• Panobinostat in combination with bortezomib and dexamethasone</li> </ul>

	<p>For people who have had 3 previous therapies:</p> <ul style="list-style-type: none"> <li>• Panobinostat in combination with bortezomib and dexamethasone</li> <li>• Pomalidomide in combination with dexamethasone</li> <li>• Daratumumab monotherapy (subject to ongoing NICE appraisal)</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rates</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<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 will be taken into account.</p>
<b>Other considerations</b>	<p>If the evidence allows, subgroups based on the number of previous lines of therapy will be considered.</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>
<b>Related NICE recommendations and NICE Pathways</b>	<p><b>Related Technology Appraisals:</b></p> <p>‘Carfilzomib for previously treated multiple myeloma’ NICE Technology Appraisal. Review date July 2020</p> <p>‘Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and</p>

	<p>bortezomib' (2017). NICE Technology Appraisal 985. Review date January 2020.</p> <p>'Panobinostat for treating multiple myeloma after at least 2 previous treatments' (2016). NICE Technology Appraisal 380. Review date January 2019.</p> <p>'Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy' (2009). NICE Technology Appraisal 171. Static list.</p> <p>'Bortezomib monotherapy for relapsed multiple myeloma' (2007). NICE Technology Appraisal 129. Static list.</p> <p><b>Appraisals in development (including suspended appraisals):</b></p> <p>'Daratumumab for treating relapsed and refractory multiple myeloma' NICE technology appraisals guidance [ID933]. Publication date to be confirmed.</p> <p>'Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma' Guidance terminated.</p> <p>'Lenalidomide for treating multiple myeloma after 1 prior treatment with bortezomib'. Part review of TA171. NICE technology appraisals guidance [ID667]. (suspended appraisal).</p> <p><b>Related Guidelines:</b></p> <p>'Myeloma: diagnosis and management of myeloma' (2016). NICE guideline 35. Review date to be confirmed.</p> <p>'Haematological cancers – improving outcomes' (2016) NICE guideline 47 Review date to be confirmed.</p> <p><b>Related NICE Pathways:</b></p> <p>Blood and bone marrow cancers</p> <p><a href="http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers">http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers</a></p>
<p><b>Related National Policy</b></p>	<p>NHS England (2015) National Cancer Drugs Fund List v.6.1: <a href="https://www.england.nhs.uk/wp-content/uploads/2016/02/ncdf-list-01-02-16.pdf">https://www.england.nhs.uk/wp-content/uploads/2016/02/ncdf-list-01-02-16.pdf</a></p> <p>Independent Cancer Taskforce (2015) <a href="#">Achieving world-class cancer outcomes: a strategy for England 2015-2020</a></p> <p>NHS England (2016) <a href="#">Manual for Prescribed Specialised Services 2016/17</a> Chapter 29, Blood and marrow transplantation services (all ages).</p>

	Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1, 4 and 5. <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a>
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## References

- 1 Cancer Research UK 'Myeloma incidence by sex and UK region'. Accessed July 2017.
- 2 Cancer Research UK 'Myeloma incidence'. Accessed May 2016.
- 3 Cancer Research UK 'Myeloma survival'. Accessed May 2016.