

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (CDF review of TA510)

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of daratumumab within its marketing authorisation for treating relapsed and 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 2013, 4,703 people were diagnosed with multiple myeloma in England.¹ Forty-three percent of people diagnosed are aged 75 years and over.¹ 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.¹ 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. Following initial treatment, subsequent therapy is influenced by previous treatment and response to it, duration of remission, comorbidities and patient preference. NICE technology appraisal guidance 129 recommends bortezomib monotherapy as an option for treating progressive multiple myeloma in people who are at first relapse having received 1 prior therapy and who have undergone, or are unsuitable for bone marrow transplantation. NICE technology appraisal guidance 171 recommends lenalidomide in combination with dexamethasone as a treatment option for people with multiple myeloma who have received at least 2 prior therapies. NICE technology appraisal guidance 380 recommends panobinostat in combination with bortezomib and dexamethasone as an option for treating multiple myeloma in adults with relapsed and/or refractory multiple myeloma who have received at least 2

prior regimens including bortezomib and an immunomodulatory agent. 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. For people who have had at least 3 prior therapies, treatment options include bendamustine (available through the Cancer Drugs Fund) or combination chemotherapy regimens (for example, alkylating agents such as melphalan and cyclophosphamide). Other subsequent treatment options may include repeating high-dose chemotherapy or chemotherapy with alkylating agents and anthracyclines, thalidomide and corticosteroids. Daratumumab monotherapy is recommended for use in the Cancer Drugs Fund for adults with relapsed and refractory multiple myeloma that has previously been treated with 3 treatments including a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy (NICE TA510).

The technology

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

Daratumumab has a marketing authorisation in the UK for treating adults with relapsed and refractory multiple myeloma, whose prior therapy included a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy.

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| Intervention(s) | Daratumumab |
| Population(s) | Adults with relapsed and refractory multiple myeloma that has previously been treated with 3 treatments including a proteasome inhibitor and an immunomodulatory agent and who have demonstrated disease progression on the last therapy |
| Comparators | <ul style="list-style-type: none"> • Panobinostat with bortezomib and dexamethasone • Lenalidomide with dexamethasone • Pomalidomide with 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) |

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| Outcomes | <p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • progression-free survival • overall survival • response rates • time to next treatment • adverse effects of treatment • health-related quality of life. |
| Economic analysis | <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> |
| Other considerations | <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> |
| Related NICE recommendations and NICE Pathways | <p>Related Technology Appraisals:</p> <p>Carfilzomib with dexamethasone and lenalidomide for previously treated multiple myeloma (2021) NICE technology appraisal guidance 695. Review date expected 2024.</p> <p>Isatuximab with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (2020) NICE technology appraisal guidance 658. Review date expected 2023.</p> <p>Carfilzomib for previously treated multiple myeloma. (2020) NICE technology appraisal guidance 657. Review date expected 2023.</p> <p>Lenalidomide plus dexamethasone for multiple myeloma</p> |

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| | <p>after 1 treatment with bortezomib. (2019) NICE technology appraisal guidance 586. Review date expected 2022.</p> <p>Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma. (2019) NICE technology appraisal guidance 573. Review date expected 2021.</p> <p>Daratumumab monotherapy for treating relapsed and refractory multiple myeloma. (2018) NICE technology appraisal guidance 510.</p> <p>Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma. (2018) NICE technology appraisal guidance 505. Review date expected December 2019.</p> <p>Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (2017) NICE technology appraisal guidance 427. Review date to be confirmed.</p> <p>Panobinostat for treating multiple myeloma after at least 2 previous treatments. (2016) NICE technology appraisal guidance 380. Reviewed January 2019.</p> <p>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.</p> <p>Bortezomib monotherapy for relapsed multiple myeloma. (2007) NICE technology appraisal guidance 129. Guidance on static list 2012.</p> <p>Terminated appraisals</p> <p>Selinexor with low-dose dexamethasone for treating refractory multiple myeloma (terminated appraisal) (2021) NICE technology appraisal guidance 700.</p> <p>Pomalidomide with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2019) NICE technology appraisal guidance 602.</p> <p>Bortezomib for treating multiple myeloma after second or subsequent relapse (terminated appraisal) (2017) NICE technology appraisal guidance 453.</p> <p>Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2017) NICE technology appraisal</p> |
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| | <p>guidance 454.</p> <p>Elotuzumab for previously treated multiple myeloma (terminated appraisal) (2017) NICE technology appraisal guidance 434.</p> <p>Multiple myeloma - carfilzomib (with lenalidomide and dexamethasone, after prior therapy) (terminated appraisal) (2016) [ID677].</p> <p>Appraisals in development (including suspended appraisals)</p> <p>Carfilzomib with daratumumab and dexamethasone for treating relapsed or refractory multiple myeloma [ID2709] Publication date October 2022.</p> <p>Idecabtagene vicleucel for treating relapsed and refractory multiple myeloma in people who have received at least 3 prior therapies [ID1442] Publication date to be confirmed.</p> <p>Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma [ID3797] Publication date to be confirmed.</p> <p>Belantamab mafodotin for treating relapsed or refractory multiple myeloma after 3 therapies [ID2701] Publication date to be confirmed.</p> <p>Elotuzumab for multiple myeloma [ID966] (suspended).</p> <p>Isatuximab with carfilzomib and dexamethasone for treating relapsed or refractory multiple myeloma [ID1620] (suspended).</p> <p>Elotuzumab with pomalidomide and dexamethasone for treating multiple myeloma after 2 therapies [ID1467] (suspended).</p> <p>Multiple myeloma (one prior therapy) - vorinostat (with bortezomib) [ID501] (suspended).</p> <p>Pembrolizumab for previously treated multiple myeloma [ID1139] (suspended).</p> <p>Plitidepsin in combination with dexamethasone for treating relapsed or refractory multiple myeloma [ID1081] (suspended).</p> <p>Daratumumab with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma [ID3775] (suspended).</p> <p>Pelareorep for treating relapsed or refractory multiple myeloma [ID1028] (suspended).</p> |
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| | <p>Related Guidelines:</p> <p>COVID-19 rapid guideline: delivery of systemic anticancer treatments (2020) NICE guideline NG161</p> <p>Myeloma: diagnosis and management (2016). NICE guideline 35. Review date February 2019.</p> <p>Haematological cancers – improving outcomes (2016) NICE guideline 47 Review date to be confirmed.</p> <p>Related Quality Standards:</p> <p>Haematological cancers (2017) NICE quality standard 150</p> <p>Related NICE Pathways:</p> <p>Myeloma (2017) NICE pathway</p> |
| <p>Related National Policy</p> | <p>The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Blood and marrow transplantation services (adults and children) [section 29, pages 98-100]</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2, 4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p> <p>Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020</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.