

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Daratumumab in combination for untreated multiple myeloma when stem cell transplant is suitable

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of daratumumab with bortezomib, thalidomide and dexamethasone within its marketing authorisation for untreated multiple myeloma when stem cell transplant is suitable.

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 2017, 5,034 people were diagnosed with multiple myeloma in England.¹ It is most frequently diagnosed in older people, with 44% of new cases in England in people 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.² The 5-year survival rate for adults with multiple myeloma in England is about 56%.³

Treatment aims to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. Autologous stem cell transplantation may be an option for some people with multiple myeloma. For those people, [NICE technology appraisal 311](#) recommends induction therapy with bortezomib in combination with either dexamethasone or dexamethasone and thalidomide, before high-dose chemotherapy and autologous stem cell transplantation. There are no approved consolidation or maintenance treatments currently available after transplant, however letermovir is recommended in [NICE technology appraisal 591](#) for preventing cytomegalovirus disease. Lenalidomide is currently undergoing NICE appraisal for use as maintenance treatment post-transplant.

The technology

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

Daratumumab in combination with bortezomib, thalidomide and dexamethasone has

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a marketing authorisation for the treatment of adults with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant.

Intervention(s)	Daratumumab with bortezomib, thalidomide and dexamethasone
Population(s)	People with previously untreated multiple myeloma who are eligible for autologous stem cell transplantation
Comparators	<ul style="list-style-type: none"> • Bortezomib with dexamethasone or with dexamethasone and thalidomide • Bortezomib with cyclophosphamide and dexamethasone (off-label) • Cyclophosphamide with thalidomide and dexamethasone (off-label)
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • overall survival • progression-free survival • response rate • minimal residual disease-negative status • proportion of people undergoing high dose chemotherapy and autologous stem cell transplantation • 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 will be taken into account.</p> <p>The availability and cost of generic products should be taken into account.</p>
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

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	the regulator.
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>Bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation (2014) NICE technology appraisal 311. Guidance on static list.</p> <p>Letermovir for preventing cytomegalovirus disease after a stem cell transplant (2019) NICE technology appraisal 591. Review date 2022.</p> <p>Terminated appraisals:</p> <p>Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal). NICE technology appraisal 454.</p> <p>Lenalidomide with bortezomib and dexamethasone for untreated multiple myeloma (terminated appraisal). NICE technology appraisal 603.</p> <p>Appraisals in development (including suspended appraisals):</p> <p>Lenalidomide for the maintenance treatment of multiple myeloma after autologous stem cell transplantation. NICE technology appraisal ID475. Publication expected 28 October 2020.</p> <p>Daratumumab with lenalidomide and dexamethasone for untreated multiple myeloma NICE technology appraisal ID1352. Suspended.</p> <p>Related Guidelines:</p> <p>‘Myeloma: diagnosis and management of myeloma’ (2016, updated 2018). NICE guideline 35.</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>
Related National Policy	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Blood and marrow transplantation services (adults and children) [section 29, page 79]</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 4, 5.</p>

References

1. Cancer Research UK. [‘Myeloma incidence statistics’](#). Accessed June 2020.

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2. National cancer institute '[Cancer Stat Facts: Myeloma](#)'. Accessed June 2020.
3. Cancer Research UK '[Myeloma survival](#)'. Accessed June 2020.