NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Daratumumab with bortezomib, lenalidomide and dexamethasone for untreated multiple myeloma when an autologous stem cell transplant is suitable

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of daratumumab with bortezomib, lenalidomide and dexamethasone within its marketing authorisation for untreated multiple myeloma when high-dose chemotherapy and autologous stem cell transplant are 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 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 (as a result of anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems**.**

There were almost 5,000 newly diagnosed cases of multiple myeloma in England in 2020.[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 and Wales is about 55%.[3] 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. High-dose chemotherapy with autologous stem-cell transplantation may be an option for some people with multiple myeloma in good general health.

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 and NICE technology appraisal 763 recommends daratumumab in combination with bortezomib, thalidomide and dexamethasone for untreated multiple myeloma in adults, when an autologous stem cell transplant is suitable. NICE technology appraisal 680 recommends lenalidomide as maintenance treatment after an autologous stem cell transplant for newly diagnosed multiple myeloma in adults.

The technology

Daratumumab (Darzalex, Janssen) with bortezomib, lenalidomide and dexamethasone does not currently have a marketing authorisation for untreated multiple myeloma when high-dose chemotherapy and autologous stem cell transplant are suitable. It has been studied in a clinical trial in combination with bortezomib, lenalidomide and dexamethasone compared with bortezomib, lenalidomide and

dexamethasone in adults with newly diagnosed multiple myeloma who are eligible for high-dose therapy and autologous stem cell transplantation.

Daratumumab in combination with bortezomib, thalidomide and dexamethasone has a marketing authorisation for the treatment of adults with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant.

Intervention(s)	Daratumumab in combination with bortezomib, lenalidomide and dexamethasone
Population(s)	Adults with newly diagnosed multiple myeloma who are eligible for high-dose chemotherapy with autologous stem cell transplant
Comparators	• Bortezomib with dexamethasone or with dexamethasone and thalidomide • Bortezomib with cyclophosphamide and dexamethasone (off-label) • Cyclophosphamide with thalidomide and dexamethasone (off-label) • Daratumumab with bortezomib, thalidomide and dexamethasone
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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	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:** Daratumumab in combination for untreated multiple myeloma when a stem cell transplant is suitable (2022) NICE technology appraisal guidance 763. Bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation (2014) NICE technology appraisals guidance 311. Lenalidomide maintenance treatment after an autologous stem cell transplant for newly diagnosed multiple myeloma (2021) NICE technology appraisals guidance 680. **Related NICE guidelines:** Myeloma: diagnosis and management of myeloma (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 (2018) NHS manual for prescribed specialist services (2018/2019) Chapter 29 Haematopoietic stem cell transplantation services (adults and children)

	Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 4, 5.

Questions for consultation

Where do you consider daratumumab in combination will fit into the existing care pathway for multiple myeloma?

Please select from the following, will insert the technology be:

A. Prescribed in primary care with routine follow-up in primary care

B. Prescribed in secondary care with routine follow-up in primary care

C. Prescribed in secondary care with routine follow-up in secondary care

D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would daratumumab in combination be a candidate for managed access?

Do you consider that the use of daratumumab in combination can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which daratumumab in combination will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE is considering evaluating this technology through its cost comparison evaluation process.
Please provide comments on the appropriateness of appraising this topic through this process.

(Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?
- Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.
- Will the intervention be used to treat the same population as the comparator(s)?
- Overall is the technology likely to offer similar or improved health benefits compared with the comparators?
- Would it be appropriate to use the cost-comparison methodology for this topic?

References

1. NHS Digital 'Cancer registration statistics, England, 2020'. [accessed February, 2025]
2. Cancer Research UK 'Myeloma'. [accessed, February 2025]
3. Cancer Research UK 'Survival for Myeloma'. [accessed, February 2025]

