Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Daratumumab with bortezomib, lenalidomide and dexamethasone for untreated multiple myeloma when a stem cell transplant is unsuitable

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 stem cell transplant is unsuitable.

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 supress 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.[1]

There were around 5,000 newly diagnosed cases of multiple myeloma in England in 2021, mostly in people aged 65 years and over.[2] Multiple myeloma is more common in men than in women.[2] The 5-year survival rate for adults with multiple myeloma in England and Wales is about 56%.[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 people with multiple myeloma in good general health; however, this is an intensive treatment, which is not considered appropriate for most people with multiple myeloma.

NICE technology appraisal guidance 917 (TA917) recommends daratumumab with lenalidomide and dexamethasone as an option for untreated multiple myeloma in adults when an autologous stem cell transplant is unsuitable.

NICE technology appraisal guidance 228 (TA228) recommends thalidomide in combination with an alkylating agent and a corticosteroid for the first-line treatment of multiple myeloma in people for whom high-dose chemotherapy with stem cell transplantation is considered inappropriate. However, thalidomide-based combinations are no longer regularly used in NHS practice, as outlined by clinical experts in NICE technology appraisal guidance 917. If the person is unable to tolerate or has contraindications to thalidomide, treatment options include bortezomib in combination with an alkylating agent and a corticosteroid (NICE technology appraisal guidance 228), and lenalidomide plus dexamethasone (NICE technology appraisal guidance 587).

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The technology

Daratumumab (Darzalex, Janssen) with bortezomib, lenalidomide and dexamethasone (also known as D-VRd) does not currently have a marketing authorisation in the UK for treating newly diagnosed multiple myeloma when a stem cell transplant is unsuitable. It has been studied in a clinical trial in people with untreated multiple myeloma, including those for whom stem cell transplant is not planned as initial therapy. The trial compared D-VRd with treatment with bortezomib, lenalidomide and dexamethasone (also known as VRd).

Intervention(s)	Daratumumab with bortezomib, lenalidomide and dexamethasone
Population(s)	Adults with untreated multiple myeloma when a stem cell transplant is unsuitable
Comparators	• Daratumumab with lenalidomide and dexamethasone • Lenalidomide with dexamethasone • Bortezomib with alkylating agent and corticosteroid (such as cyclophosphamide and dexamethasone) • Isatuximab with bortezomib, lenalidomide and dexamethasone (subject to NICE evaluation)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • time to treatment discontinuation • minimal residual disease-negative status • adverse effects of treatment • health-related quality of life.

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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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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.
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 with lenalidomide and dexamethasone for untreated multiple myeloma when a stem cell transplant is unsuitable (2023) NICE technology appraisal guidance 917. Daratumumab in combination for untreated multiple myeloma when a stem cell transplant is suitable (2022) NICE technology appraisal guidance 763. Lenalidomide plus dexamethasone for previously untreated multiple myeloma (2019) NICE technology appraisal guidance 587. Bortezomib and thalidomide for the first-line treatment of multiple myeloma (2011) NICE technology appraisal guidance 228. **Related technology appraisals in development:** Isatuximab in combination for untreated multiple myeloma when a stem cell transplant is unsuitable NICE technology appraisal guidance [ID3981] Publication expected July 2025. **Related NICE guidelines:** Myeloma: diagnosis and management (2016, updated 2018). NICE guideline 35.

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	Haematological cancers: improving outcomes (2016). NICE guidance 47. **Related quality standards:** Haematological cancers (2017) NICE quality standard 150.

Questions for consultation

Have all the relevant comparators been included in the scope?

Are thalidomide combination treatments still commonly used in NHS practice in England for multiple myeloma when stem cell transplant is unsuitable? Would bortezomib with an alkylating agent and corticosteroid or lenalidomide with dexamethasone ever be used as a first line treatment where thalidomide combination treatments could be tolerated or was not contraindicated?

Which factors drive treatment decisions when deciding between offering bortezomib with an alkylating agent and corticosteroid or lenalidomide with dexamethasone as alternatives to daratumumab with lenalidomide and dexamethasone?

Where do you consider daratumumab with bortezomib, lenalidomide and dexamethasone will fit into the existing care pathway for multiple myeloma?

Please select from the following, will daratumumab with bortezomib, lenalidomide and dexamethasone 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 with bortezomib, lenalidomide and dexamethasone be a candidate for managed access?

Do you consider that the use of daratumumab with bortezomib, lenalidomide and dexamethasone 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 with bortezomib, lenalidomide and dexamethasone 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;

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- 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. Cancer Research UK (2023) Myeloma. Accessed February 2025

2. NHS Digital (2023) Cancer registration statistics, 2021. Accessed February 2025

3. NHS Digital (2023) Cancer Survival in England, cancers diagnosed 2016 to 2020, followed up to 2021. Accessed March 2024

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