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

Final scope

Final 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 as a subcutaneous formulation 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).

Daratumumab with bortezomib, lenalidomide and dexamethasone for untreated multiple myeloma when an autologous stem cell transplant is suitable is a related technology appraisal in development.

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 negativity • 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.

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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:** Daratumumab with bortezomib, lenalidomide and dexamethasone for untreated multiple myeloma when an autologous stem cell transplant is suitable is a related technology appraisal in development. NICE technology appraisal guidance [ID6249] Expected publication date TBC. 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. Haematological cancers: improving outcomes (2016). NICE guidance 47. **Related quality standards:** Haematological cancers (2017) NICE quality standard 150.

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