NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

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

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of daratumumab with 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 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 5,041 newly diagnosed cases of multiple myeloma in England in 2019.[1] Fifty-nine percent of people diagnosed in the UK are aged 70 years and over. 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 52%.[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 228 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 when stem cell transplantation is considered inappropriate. 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).

The technology

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

Daratumumab in combination with lenalidomide and dexamethasone or with bortezomib, melphalan and prednisone has a marketing authorisation in the UK for treating adults with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant.

Intervention	Daratumumab with lenalidomide and dexamethasone
Population	Adults with untreated multiple myeloma when stem cell transplant is unsuitable
Comparators	• Thalidomide with alkylating agent and corticosteroid For people who are unable to tolerate, or have contraindications to thalidomide: • Bortezomib with alkylating agent and corticosteroid • Lenalidomide with dexamethasone
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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 or comparator technologies will be taken into account. The availability and cost of biosimilar 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 and NICE Pathways	**Related Technology Appraisals:** Carfilzomib with dexamethasone and lenalidomide for previously treated multiple myeloma (2021) NICE technology appraisal guidance 695. Review date expected 2024. Isatuximab with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (2020) NICE technology appraisal guidance 658. Review date expected 2023. Carfilzomib for previously treated multiple myeloma. (2020) NICE technology appraisal guidance 657. Review date expected 2023. Lenalidomide plus dexamethasone for multiple myeloma after 1 treatment with bortezomib. (2019) NICE technology appraisal guidance 586. Review date expected 2022. Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma. (2019) NICE technology appraisal guidance 573. Review date expected 2021. Daratumumab monotherapy for treating relapsed and refractory multiple myeloma. (2018) NICE technology appraisal guidance 510. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma. (2018) NICE technology appraisal guidance 505. Review date expected December 2019. Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (2017) NICE technology appraisal guidance 427. Review date to be confirmed. Panobinostat for treating multiple myeloma after at least 2 previous treatments. (2016) NICE technology appraisal guidance 380. Reviewed January 2019. 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. Bortezomib monotherapy for relapsed multiple myeloma. (2007) NICE technology appraisal guidance 129. Guidance on static list 2012.. **Terminated appraisals**

	Selinexor with low-dose dexamethasone for treating refractory multiple myeloma (terminated appraisal) (2021) NICE technology appraisal guidance 700. Pomalidomide with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2019) NICE technology appraisal guidance 602. Bortezomib for treating multiple myeloma after second or subsequent relapse (terminated appraisal) (2017) NICE technology appraisal guidance 453. Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2017) NICE technology appraisal guidance 454. Elotuzumab for previously treated multiple myeloma (terminated appraisal) (2017) NICE technology appraisal guidance 434. Multiple myeloma - carfilzomib (with lenalidomide and dexamethasone, after prior therapy) (terminated appraisal) (2016) [ID677]. **Appraisals in development (including suspended appraisals)** Carfilzomib with daratumumab and dexamethasone for treating relapsed or refractory multiple myeloma [ID2709] Publication date October 2022. 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. Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma [ID3797] Publication date to be confirmed. Belantamab mafodotin for treating relapsed or refractory multiple myeloma after 3 therapies [ID2701] Publication date to be confirmed. Elotuzumab for multiple myeloma [ID966] (suspended). Isatuximab with carfilzomib and dexamethasone for treating relapsed or refractory multiple myeloma [ID1620] (suspended). Elotuzumab with pomalidomide and dexamethasone for treating multiple myeloma after 2 therapies [ID1467] (suspended). Multiple myeloma (one prior therapy) - vorinostat (with

	bortezomib) [ID501] (suspended). Pembrolizumab for previously treated multiple myeloma [ID1139] (suspended). Plitidepsin in combination with dexamethasone for treating relapsed or refractory multiple myeloma [ID1081] (suspended). Daratumumab with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma [ID3775] (suspended). Pelareorep for treating relapsed or refractory multiple myeloma [ID1028] (suspended). **Related Guidelines:** COVID-19 rapid guideline: delivery of systemic anticancer treatments (2020) NICE guideline NG161 Myeloma: diagnosis and management (2016). NICE guideline 35. Review date February 2019. Haematological cancers – improving outcomes (2016) NICE guideline 47 Review date to be confirmed. **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 (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 to 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for daratumumab with lenalidomide and dexamethasone been included in the scope?

- Which treatments are considered to be established clinical practice in the NHS for untreated multiple myeloma when stem cell transplant is unsuitable?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom daratumumab with lenalidomide and dexamethasone is expected to be more clinically effective and cost effective or other groups that should be examined separately?

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 lenalidomide and dexamethasone is 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.

Do you consider daratumumab with lenalidomide and dexamethasone to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of daratumumab with lenalidomide and dexamethasone can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Evaluation (STE) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at.
https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation

References

1. Cancer Research UK, Myeloma incidence statistics. Accessed February 2022.

2. Cancer Research UK 'Myeloma incidence'. Accessed February 2022.

3. Cancer Research UK 'Myeloma survival'. Accessed February 2022.