Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Daratumumab in combination with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma (Review of TA573)

Final scope

Remit

To appraise the clinical and cost effectiveness of daratumumab in combination with bortezomib and dexamethasone within its marketing authorisation for treating relapsed or refractory multiple myeloma.

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 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.

In 2014, 5,034 people were diagnosed with multiple myeloma in England 2017.[1] Of these, 43% are 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 52%.[2]

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. If the disease progresses after initial treatment, the choice of subsequent therapy is influenced by previous treatment and response to it, duration of remission, comorbidities and patient preference.

For people whose disease is relapsed or refractory after at least 1 prior therapy:

- NICE technology appraisal guidance 129 recommends bortezomib monotherapy as an option for people who are at first relapse having had 1 prior therapy and who have undergone, or are unsuitable for bone marrow transplantation.

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- NICE technology appraisal guidance 657 recommends carfilzomib in combination with dexamethasone as an option for treating multiple myeloma in adults, only if they have had only 1 previous therapy, which did not include bortezomib.

- NICE technology appraisal guidance 171 recommends lenalidomide in combination with dexamethasone as an option for the treatment of multiple myeloma in people who have received 2 or more prior therapies.

- NICE technology appraisal guidance 380 recommends panobinostat in combination with bortezomib and dexamethasone as a treatment option for people with relapsed and refractory multiple myeloma who have received at least 2 prior therapies including bortezomib and an immunomodulatory agent.

- NICE technology appraisal guidance 427 recommends pomalidomide in combination with dexamethasone as an option for treating multiple myeloma in adults after 3 previous treatments including both lenalidomide and bortezomib.

- NICE technology appraisal guidance 783 recommends daratumumab monotherapy as an option for treating relapsed and refractory multiple myeloma in adults who have had 3 previous therapies including a proteasome inhibitor and an immunomodulator.

The technology

Daratumumab (Darzalex, Janssen-Cilag) in combination with bortezomib and dexamethasone has a marketing authorisation in the UK for the treatment of adult patients with multiple myeloma who have received at least 1 prior therapy.

Intervention(s)	Daratumumab in combination with bortezomib and dexamethasone.
Population(s)	Adults with relapsed or refractory multiple myeloma who have had at least 1 previous therapy.
Subgroups	If the evidence allows, subgroups based on the number of previous lines of therapy will be considered.
Comparators	For people who have had 1 previous therapy, depending on previous therapy: • Bortezomib-based therapy • Carfilzomib in combination with dexamethasone • Combination chemotherapy

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	For people who have had 2 previous therapies: • Lenalidomide in combination with dexamethasone • Panobinostat in combination with bortezomib and dexamethasone For people who have had 3 previous therapies: • Panobinostat in combination with bortezomib and dexamethasone • Pomalidomide in combination with dexamethasone • Daratumumab monotherapy
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • time to next treatment • 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 of any managed access arrangement for the intervention will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.
Other considerations	If the evidence allows, subgroups based on the number of previous lines of therapy will be considered. 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.

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Related NICE recommendations	**Related Technology Appraisals:** Daratumumab monotherapy for treating relapsed and refractory multiple myeloma. (2022) NICE technology appraisal guidance 783. Review date expected 2025. Carfilzomib with dexamethasone and lenalidomide for previously treated multiple myeloma. (2021) NICE technology appraisal guidance TA695. Review date expected 2024. Carfilzomib for previously treated multiple myeloma. (2020) NICE technology appraisal guidance 657. Review date expected 2023. Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma. (2020) NICE technology appraisal guidance TA658. 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. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma. (2018) NICE technology appraisal guidance 505. Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (2017) NICE technology appraisal guidance 427. Review date expected 2020. Panobinostat for treating multiple myeloma after at least 2 previous treatments. (2016) NICE technology appraisal guidance 380. Reviewed January 2019, nothing new was found that affects the recommendations. Lenalidomide for the treatment of multiple myeloma in people who have received at least 2 prior therapies. (2009) NICE technology appraisal guidance 171. Last updated June 2019. Bortezomib monotherapy for relapsed multiple myeloma. (2007) NICE technology appraisal guidance 129. Reviewed November 2012, nothing new was found that affects the recommendations. **Related appraisals in development:** Carfilzomib with daratumumab and dexamethasone for treating relapsed or refractory multiple myeloma [ID2709] NICE technology appraisal. Publication expected October 2022. Elotuzumab for multiple myeloma [ID966] NICE technology appraisal. Publication date to be confirmed. Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma [ID3797] NICE technology appraisal. Publication date to be confirmed. Idecabtagene vicleucel for treating relapsed and refractory multiple myeloma in people who have received at least 3 prior

	therapies [ID1442] NICE technology appraisal. Publication date to be confirmed. Ciltacabtagene autoleucel for treating relapsed or refractory multiple myeloma [ID3816] NICE technology appraisal. Publication date to be confirmed. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (CDF review of TA505) [ID1635] NICE technology appraisal. Publication date to be confirmed. Belantamab mafodotin for treating relapsed or refractory multiple myeloma after 3 therapies [ID2701] NICE technology appraisal. Publication date to be confirmed. Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma [Review of TA658] [ID4067] NICE technology appraisal. Publication date to be confirmed. **Related Guidelines:** Haematological cancers: improving outcomes (2016) NICE guideline 47 Myeloma: diagnosis and management (2016) NICE guideline 35. **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) Blood and marrow transplantation services (adults and children) [section 29, pages 98-100]**Error! Hyperlink reference not valid.** Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2, 4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017**Error! Hyperlink reference not valid.**