NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Daratumumab for treating relapsed or refractory multiple myeloma

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of daratumumab with lenalidomide and dexamethasone, and daratumumab 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 2013, 4,703 people were diagnosed with multiple myeloma in England[i]. 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[ii]. The 5-year survival rate for adults with multiple myeloma in England and Wales is about 47%[iii].

Multiple myeloma is an incurable disease. The main aims of therapy are 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. 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. NICE technology appraisal guidance 171 recommends lenalidomide in combination with dexamethasone as a treatment option for people who have had at least 2 prior therapies. NICE technology appraisal guidance 380 recommends panobinostat in combination with bortezomib and dexamethasone as an option for adults with relapsed or refractory disease who have had at least 2 prior regimens including bortezomib and an

immunomodulatory agent (thalidomide or lenalidomide). Other subsequent treatment options may include repeating high-dose chemotherapy or chemotherapy with alkylating agents and anthracyclines, thalidomide and corticosteroids. NICE technology appraisal guidance 338 does not recommend pomalidomide in combination with dexamethasone for treating multiple myeloma in adults who have had at least 2 previous treatments.

The technology

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

Daratumumab monotherapy has a marketing authorisation in the UK for treating adults with relapsed and refractory multiple myeloma previously treated with a proteasome inhibitor and an immunomodulatory agent, whose disease progressed on the last therapy. Daratumumab in combination with other drugs does not currently have a marketing authorisation in the UK. It has been studied in clinical trials in combination with lenalidomide and dexamethasone compared with lenalidomide and dexamethasone alone, and in combination with bortezomib and dexamethasone compared with bortezomib and dexamethasone alone, in adults with relapsed or refractory multiple myeloma who have had at least 1 prior therapy and have evidence of disease progression.

Intervention(s)	Daratumumab with lenalidomide and dexamethasone Daratumumab with bortezomib and dexamethasone
Population(s)	Adults with relapsed or refractory multiple myeloma
Comparators	For people who have had 1 prior therapy: • Bortezomib • Lenalidomide with dexamethasone (subject to ongoing NICE appraisal) • Carfilzomib with dexamethasone or lenalidomide and dexamethasone (subject to ongoing NICE appraisal). For people who have had at least 2 prior therapies: • Lenalidomide with dexamethasone • Panobinostat with bortezomib and dexamethasone • Carfilzomib with dexamethasone or lenalidomide and dexamethasone (subject to ongoing NICE appraisal) • Pomalidomide with dexamethasone (subject to

	ongoing NICE appraisal).
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 patient access schemes for the intervention or comparator technologies will be taken into account. The availability and cost of biosimilars 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: 'Panobinostat for treating multiple myeloma after at least 2 previous treatments' (2016). NICE Technology Appraisal 380. Review date January 2019. 'Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib' (2015). NICE Technology Appraisal 338. Review date March 2018. 'Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy' (2009). NICE Technology Appraisal 171. Static list. 'Bortezomib monotherapy for relapsed multiple

	myeloma' (2007). NICE Technology Appraisal 129. Static list. Appraisals in development (including suspended appraisals): 'Daratumumab for treating relapsed and refractory multiple myeloma' NICE technology appraisals guidance [ID933]. Publication date TBC. 'Carflizomib for previously treated multiple myeloma' NICE technology appraisals guidance [ID934]. Publication expected April 2017. 'Multiple myeloma (relapsed, refractory) – pomalidomide (after lenalidomide and bortezomib)' NICE technology appraisals guidance [ID985]. Publication expected April 2017. 'Lenalidomide for treating multiple myeloma after 1 prior treatment with bortezomib'. Part review of TA171. NICE technology appraisals guidance [ID667]. (suspended appraisal). 'Elotuzumab for treating relapsed or refractory multiple myeloma' Proposed NICE technology appraisal [ID855]. (suspended appraisal). Related Guidelines: 'Myeloma: diagnosis and management of myeloma' (2016). NICE guideline 35. Review date to be confirmed. 'Haematological cancers – improving outcomes' (2016) NICE guideline 47 Review date to be confirmed. Related NICE Pathways: Blood and bone marrow cancers http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers
Related National Policy	NHS England (2015) National Cancer Drugs Fund List v.6.1: https://www.england.nhs.uk/wp-content/uploads/2016/02/ncdf-list-01-02-16.pdf Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 NHS England (2016) Manual for Prescribed Specialised Services 2016/17 Chapter 29, Blood and marrow transplantation services (all ages). Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 1, 4 and 5.

	https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

NICE intends to jointly appraise both daratumumab with lenalidomide and dexamethasone and daratumumab with bortezomib and dexamethasone through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising both these topics through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

Have all relevant comparators for daratumumab with lenalidomide and dexamethasone and daratumumab with bortezomib and dexamethasone been included in the scope? Which treatments are considered to be established clinical practice in the NHS for relapsed or refractory multiple myeloma?

Are the outcomes listed appropriate?

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

Where do you consider daratumumab will fit into the existing NICE pathway, blood and bone marrow cancers?

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 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.

Do you consider daratumumab with lenalidomide and dexamethasone and daratumumab with bortezomib and dexamethasone to be innovative in their potential to make a significant and substantial impact on health-related benefits and how they 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 and daratumumab with bortezomib 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.

References

[i] Cancer Research UK 'Myeloma incidence by sex and UK region'. Accessed May 2016.
[ii] Cancer Research UK 'Myeloma incidence'. Accessed May 2016.
[iii] Cancer Research UK 'Myeloma survival'. Accessed May 2016.