NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Daratumumab for treating relapsed and refractory multiple myeloma

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of daratumumab within its marketing authorisation for treating relapsed and 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 2012, 4190 people were diagnosed with multiple myeloma in England[i]. It is most frequently diagnosed in older people, with 43% [ii]of people diagnosed aged 75 years and over between 2009 and 2011. Multiple myeloma is more common in men than in women and the incidence is also reported to be higher in people of African and Caribbean family origin. There were 2303[iii] deaths in England in 2012. The 5-year survival rate for adults with multiple myeloma in England is estimated to be 42.2%[iv].

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. Following initial treatment, 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 treating progressive multiple myeloma in people who are at first relapse having received 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 with multiple myeloma who have received at least 2 prior therapies. 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 relapsed or refractory multiple myeloma in adults who have had at least 2 previous treatments, including lenalidomide and bortezomib.

The technology

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

Daratumumab does not currently have a marketing authorisation in the UK for treating relapsed and refractory multiple myeloma. It has been studied in a single-arm clinical trial in people who had received at least 3 prior treatments including a proteasome inhibitor and an immunomodulatory agent, or whose disease was refractory to a proteasome inhibitor and an immunomodulatory agent.

Intervention(s)	Daratumumab
Population(s)	People with relapsed or refractory multiple myeloma that has previously been treated with a proteasome inhibitor and an immunomodulatory agent
Comparators	• Lenalidomide with dexamethasone • Panobinostat with bortezomib and dexamethasone (subject to ongoing NICE appraisal) • Bendamustine (not appraised by NICE but funded via the Cancer Drugs Fund; does not currently have a marketing authorisation in the UK for this indication)
Outcomes	The outcome measures to be considered include: • progression-free survival • overall 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 patient access schemes for the intervention or comparator technologies 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: 'Bortezomib monotherapy for relapsed multiple myeloma' (2007). NICE technology appraisal 129. Moved to static list, November 2012. 'Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy' (2009). NICE technology appraisal 171. Moved to static list, November 2012. 'Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib' (2015). NICE technology appraisal 338. Review date March 2018. Appraisals in development 'Panobinostat for treating multiple myeloma after at least 2 previous treatments'. NICE technology appraisal guidance [ID663]. Publication expected January 2016. 'Carfilzomib in combination with lenalidomide and dexamethasone for previously treated multiple myeloma'. NICE technology appraisals guidance [ID677]. Publication expected September 2016. 'Carfilzomib in combination with dexamethasone for previously treated multiple myeloma'. NICE technology

	appraisals guidance [ID934]. Publication date to be confirmed. 'Lenalidomide for the treatment of multiple myeloma following treatment with bortezomib' (part review of Technology Appraisal guidance 171). Suspended. Proposed appraisals 'Ixazomib citrate in combination with lenalidomide and dexamethasone for relapsed or refractory multiple myeloma'. Proposed NICE technology appraisal [ID807]. Publication date to be confirmed. 'Elotuzumab for previously treated multiple myeloma'. Proposed NICE technology appraisal [ID855]. Publication date to be confirmed. Related Guidelines: 'Myeloma: diagnosis and management of myeloma'. Publication expected February 2016. 'Improving Outcomes in Haematological Cancer' (2003). Cancer Service Guidance. NICE pathway: Blood and bone marrow cancers, Pathway created: December 2013
Related National Policy	NHS England (2014) 'Manual for prescribed specialised services 2013/14'. Chapter 29. Department of Health (2014) 'Improving Outcomes: A Strategy for Cancer, fourth annual report'. Department of Health (2014) 'NHS Outcomes Framework 2015-2016'. Domains 1, 2, 4 and 5.

Questions for consultation

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

Are the outcomes listed appropriate?

Are there any subgroups of people in whom daratumumab is 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 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 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.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) 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 http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

References

[i] Office for National Statistics (ONS) (2015) 'Registrations of newly diagnosed cases of cancer: site and sex, England, 1995 to 2012 (table 8)". Accessed November 2015

[ii] Cancer Research UK (2014) 'Myeloma incidence by age'. Accessed November 2015

[iii] Cancer Research UK (2014) 'Myeloma mortality by sex and UK region'. Accessed November 2015. Accessed November 2015

[iv] Office for National Statistics (2015) 'One-year and five-year net survival with 95% confidence intervals for adults diagnosed during 2007–2011: England, 21 common cancers by sex and age (table 2)'. Accessed November 2015.