NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Daratumumab for treating relapsed or refractory multiple myeloma [ID973]

Final scope

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 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.

Daratumumab has a marketing authorisation in the UK as a monotherapy 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. This indication is the subject of a different appraisal.

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 (with or without dexamethasone) • Lenalidomide with dexamethasone (subject to ongoing NICE appraisal) • Carfilzomib with dexamethasone or lenalidomide and dexamethasone (subject to ongoing NICE appraisal) • Conventional chemotherapy. 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). • Bendamustine (through the Cancer drugs fund) • Conventional chemotherapy.
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): 'Lenalidomide for treating multiple myeloma after 1 prior treatment with bortezomib'. Part review of TA171. NICE technology appraisals guidance [ID667]. Publication expected January 2017. '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. 'Daratumumab for treating relapsed and refractory multiple myeloma' NICE technology appraisals guidance [ID933]. Publication date July 2017. 'Ixazomib citrate in combination with lenalidomide and dexamethasone for relapsed or refractory multiple myeloma' NICE technology appraisals guidance [ID807]. Publication expected August 2017. '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

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.