NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Daratumumab in combination for untreated multiple myeloma when stem cell transplant is suitable

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of daratumumab with bortezomib, thalidomide and dexamethasone within its marketing authorisation for untreated multiple myeloma when stem cell transplant is suitable.

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 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 (due to anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems.

In 2016, 4,731 people were diagnosed with multiple myeloma in England.[1] It is most frequently diagnosed in older people, with 44% of new cases in England in people 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 and Wales is about 47%.[3]

Treatment 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 some people with multiple myeloma. For those people, NICE technology appraisal guidance 311 recommends induction therapy with bortezomib in combination with either dexamethasone or dexamethasone and thalidomide, before high-dose chemotherapy and autologous stem cell transplantation.

The technology

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

Daratumumab does not currently have a marketing authorisation for people with previously untreated multiple myeloma who are eligible for high dose chemotherapy and autologous stem cell transplantation. It has been studied in combination with bortezomib, thalidomide and dexamethasone compared with bortezomib, thalidomide and dexamethasone alone for induction (before transplantation) and consolidation (after transplantation) treatment.

Intervention(s)	Daratumumab with bortezomib, thalidomide and dexamethasone
Population(s)	People with previously untreated multiple myeloma who are eligible for stem cell transplantation
Comparators	• Bortezomib in combination with dexamethasone or with dexamethasone and thalidomide • Lenalidomide in combination with bortezomib and dexamethasone (subject to ongoing appraisal)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • proportion of people undergoing high dose chemotherapy and autologous stem cell transplantation • 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 generic 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:** Bortezomib for induction therapy in multiple myeloma before high-dose chemotherapy and autologous stem cell transplantation (2014) NICE technology appraisals guidance 311. Guidance on static list. Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (2018) NICE technology appraisal guidance 510 **Terminated appraisals:** Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal). NICE technology appraisal 454. **Appraisals in development (including suspended appraisals):** Daratumumab with lenalidomide and dexamethasone for untreated multiple myeloma [ID1352] NICE technology appraisal guidance. Publication date to be confirmed Daratumumab with bortezomib for treating relapsed or refractory multiple myeloma [ID974] NICE technology appraisal guidance. Publication date to be confirmed **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 Quality Standards:** Haematological cancers (2017) NICE quality standard 150 **Related NICE Pathways:** Myeloma (2017) NICE pathway
Related National Policy	NHS England (2017) Manual for Prescribed Specialised Services 2017/18. Blood and marrow transplantation

	services (adults and children) [section 29, page 79] Department of Health and Social Care, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 4, 5.

Questions for consultation

Have all relevant comparators for daratumumab in combination with bortezomib, thalidomide and dexamethasone been included in the scope?

Are any treatments currently used for consolidation after stem cell transplant in clinical practice in the NHS? If so, what are these?

Which first treatments are considered to be established clinical practice in the NHS for people with multiple myeloma for whom a stem cell transplant is suitable?

Are the outcomes listed appropriate?

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

Where do you consider daratumumab in combination with bortezomib, thalidomide and dexamethasone will fit into the existing NICE pathway, Myeloma?

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 in combination with bortezomib, thalidomide and dexamethasone 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 in combination with bortezomib, thalidomide 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 in combination with bortezomib, thalidomide 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 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

[1] Office of national statistics 'Cancer registration statistics, England'. Accessed November 2018.
[2] National cancer institute 'SEER Cancer Statistics Review, 1975-2008'. Accessed November 2018.
[3]Cancer Research UK 'Myeloma survival'. Accessed November 2018.