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 2017, 5,034 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 is about 56%.[3]

Treatment aims to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. Autologous stem cell transplantation may be an option for some people with multiple myeloma. For those people, NICE technology appraisal 311 recommends induction therapy with bortezomib in combination with either dexamethasone or dexamethasone and thalidomide, before high-dose chemotherapy and autologous stem cell transplantation. There are no approved consolidation or maintenance treatments currently available after transplant, however letermovir is recommended in NICE technology appraisal 591 for preventing cytomegalovirus disease. Lenalidomide is currently undergoing NICE appraisal for use as maintenance treatment post-transplant.

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 in combination with bortezomib, thalidomide and dexamethasone has a marketing authorisation for the treatment of adults with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplant .

Intervention(s)	Daratumumab with bortezomib, thalidomide and dexamethasone
Population(s)	People with previously untreated multiple myeloma who are eligible for autologous stem cell transplantation
Comparators	• Bortezomib with dexamethasone or with dexamethasone and thalidomide • Bortezomib with cyclophosphamide and dexamethasone (off-label) • Cyclophosphamide with thalidomide and dexamethasone (off-label)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • minimal residual disease-negative status • 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 appraisal 311. Guidance on static list. Letermovir for preventing cytomegalovirus disease after a stem cell transplant (2019) NICE technology appraisal 591. Review date 2022. **Terminated appraisals:** Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal). NICE technology appraisal 454. Lenalidomide with bortezomib and dexamethasone for untreated multiple myeloma (terminated appraisal). NICE technology appraisal 603. **Appraisals in development (including suspended appraisals):** Lenalidomide for the maintenance treatment of multiple myeloma after autologous stem cell transplantation. NICE technology appraisal ID475. Publication expected 28 October 2020. Daratumumab with lenalidomide and dexamethasone for untreated multiple myeloma NICE technology appraisal ID1352. Suspended. **Related Guidelines:** 'Myeloma: diagnosis and management of myeloma' (2016, updated 2018). NICE guideline 35. '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	The NHS Long Term Plan, 2019. NHS Long Term Plan 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?

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

Is consolidation treatment routinely used after transplant in the NHS? If so, what treatments are given?

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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Cancer Research UK. 'Myeloma incidence statistics'. Accessed April 2020.
2. National cancer institute 'Cancer Stat Facts: Myeloma'. Accessed April 2020.
3. Cancer Research UK 'Myeloma survival'. Accessed April 2020.