NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Carfilzomib with daratumumab and dexamethasone for treating relapsed or refractory multiple myeloma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of carfilzomib with daratumumab 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 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 (as a result of anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems.

In 2017, 4,799 people were diagnosed with multiple myeloma in England[1]. It is most frequently diagnosed in older people, with 43% 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[1, 2]. The 5-year survival rate for adults with multiple myeloma in England and Wales is about 47%[3].

Multiple myeloma is an incurable disease. Therapy aims 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.

For people whose disease is relapsed or refractory after at least 1 prior therapy:

- NICE technology appraisal guidance 129 recommends bortezomib monotherapy as an option for treating progressive multiple myeloma in people who are at first relapse and who have undergone, or are unsuitable for, bone marrow transplantation.

- NICE technology appraisal guidance 457 recommends carfilzomib plus dexamethasone as a treatment option for adults who had only 1 previous therapy which did not include bortezomib.

- NICE technology appraisal guidance 586 recommends lenalidomide plus dexamethasone as a treatment option for adults who had only 1 previous therapy which included bortezomib.

- NICE technology appraisal guidance 573 recommends daratumumab plus bortezomib and dexamethasone for use within the Cancer Drugs Fund as a treatment option for adults who have had 1 previous therapy.

For people who have had at least 2 prior therapies:

- NICE technology appraisal guidance 171 recommends lenalidomide plus dexamethasone as a treatment option for people who have had at least 2 previous therapies.

- NICE technology appraisal guidance 380 recommends panobinostat plus bortezomib and dexamethasone as a treatment option for adults who have had at least 2 previous therapies including bortezomib and an immunomodulatory agent.

- NICE technology appraisal guidance 505 recommends ixazomib citrate plus lenalidomide and dexamethasone for use within the Cancer Drugs Fund as a treatment option for adults who have had 2 or 3 previous therapies.

For people who have had at least 3 prior therapies:

- NICE technology appraisal guidance 427 recommends pomalidomide plus low-dose dexamethasone as a treatment option for adults who have had at least 3 previous treatments including both lenalidomide and bortezomib.

- NICE technology appraisal guidance 510 recommends daratumumab monotherapy for use within the Cancer Drugs Fund as a treatment option for adults who have had 3 previous therapies including a proteasome inhibitor and an immunomodulator.

The technology

Carfilzomib (Kyprolis, Amgen) is a proteasome inhibitor. By blocking proteasomes (multi-enzyme complexes that break down proteins that are no longer needed), proteins build up in the cell and cause it to die. It is administered intravenously.

Carfilzomib in combination with either lenalidomide and dexamethasone or dexamethasone alone has a marketing authorisation in the UK for treating adult patients with multiple myeloma who have received at least one prior

therapy. Carfilzomib in combination with daratumumab and dexamethasone does not currently have a marketing authorisation in the UK for treating relapsed or refractory multiple myeloma. It is being studied in a randomised trial, in adults with relapsed or progressive multiple myeloma compared with carfilzomib and dexamethasone and dexamethasone alone.

Intervention(s)	Carfilzomib in combination with daratumumab and dexamethasone
Population(s)	Adults with relapsed/refractory multiple myeloma who have had at least 1 previous therapy
Comparators	For people who have had 1 previous therapy: • bortezomib • carfilzomib plus dexamethasone • lenalidomide plus dexamethasone For people who have had 2 previous therapies: • lenalidomide plus dexamethasone • panobinostat plus bortezomib and dexamethasone For people who have had 3 or more previous therapies: • lenalidomide plus dexamethasone • panobinostat plus bortezomib and dexamethasone • pomalidomide plus dexamethasone
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rates (for example complete response) • 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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technologies appraisal guidance for the same indication a cost comparison may be carried out. 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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	If the evidence allows, subgroup analyses based on type and number of lines of previous therapy will be considered. 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:** Lenalidomide plus dexamethasone for multiple myeloma after 1 treatment with bortezomib. (2019) NICE technology appraisal guidance 586. Review date expected 2022. Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma. (2019) NICE technology appraisal guidance 573. Review date expected 2021. Daratumumab monotherapy for treating relapsed and refractory multiple myeloma. (2018) NICE technology appraisal guidance 510. Review date expected November 2020. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma. (2018) NICE technology appraisal guidance 505. Review date

	expected December 2019. Carfilzomib for previously treated multiple myeloma. (2017) NICE technology appraisal guidance 457. Review date expected July 2020. Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (2017) NICE technology appraisal guidance 427. Panobinostat for treating multiple myeloma after at least 2 previous treatments. (2016) NICE technology appraisal guidance 380. Reviewed January 2019, nothing new was found that affects the recommendations. Lenalidomide for the treatment of multiple myeloma in people who have received at least 2 prior therapies. (2009). NICE technology appraisal guidance 171. Guidance on static list 2014. Bortezomib monotherapy for relapsed multiple myeloma. (2007) NICE technology appraisal guidance 129. Guidance on static list 2012. **Terminated appraisals:** Pomalidomide with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2019) NICE technology appraisal guidance 602. Bortezomib for treating multiple myeloma after second or subsequent relapse (terminated appraisal) (2017) NICE technology appraisal guidance 453. Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2017) NICE technology appraisal guidance 454. Elotuzumab for previously treated multiple myeloma (terminated appraisal) (2017) NICE technology appraisal guidance 434. Elotuzumab for treating relapsed or refractory multiple myeloma NICE technology appraisal guidance [ID855]. (terminated appraisal). Multiple myeloma - carfilzomib (with lenalidomide and dexamethasone, after prior therapy) [ID677] NICE technology appraisal guidance. (terminated appraisal). **Appraisals in development (including suspended appraisals):**

	Selinexor with low-dose dexamethasone for treating refractory multiple myeloma [ID1535]. Publication expected January 2021. Ixazomib with lenalidomide and dexamethasone for untreated multiple myeloma [ID1170] Publication expected August 2020. Isatuximab with carfilzomib and dexamethasone for treating relapsed or refractory multiple myeloma [ID1620]. Publication expected August 2020. Isatuximab with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma [ID1477] Publication expected August 2020. Carfilzomib with dexamethasone and lenalidomide for treating multiple myeloma after at least 1 previous therapy [ID1493]. Publication date to be confirmed. Elotuzumab for multiple myeloma [ID966]. NICE technology appraisals guidance. Publication date to be confirmed. Elotuzumab with pomalidomide and dexamethasone for treating multiple myeloma after 2 therapies [ID1467]. [Suspended]. Multiple myeloma (one prior therapy) - vorinostat (with bortezomib) [ID501]. [Suspended]. Pembrolizumab for previously treated multiple myeloma [ID1139]. [Suspended]. Plitidepsin in combination with dexamethasone for treating relapsed or refractory multiple myeloma [ID1081]. [Suspended]. Pomalidomide in combination with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma [ID1358] [Suspended]. **Related Guidelines:** Haematological cancers: improving outcomes (2016) NICE guideline 47 Myeloma: diagnosis and management (2016) NICE guideline 35 **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 (2018/2019) NHS manual for prescribed specialist services (2018/2019) Blood and marrow transplantation services (adults and children) [section 29, pages 98-100] Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1,2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Which treatments are considered to be established clinical practice in the NHS for relapsed or refractory multiple myeloma?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom carfilzomib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider carfilzomib will fit into the existing NICE pathway for 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 carfilzomib 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 carfilzomib 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 carfilzomib 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]Office of national statistics 'Cancer registration statistics, England'. Accessed February 2020.

[2]National cancer institute 'SEER Cancer Statistics Review, 1975-2016'. Accessed February 2020.

[3]Cancer Research UK 'Myeloma survival'. Accessed February 2020.