

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Carfilzomib for previously treated multiple myeloma (part review of TA457) [ID1493]

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of carfilzomib plus lenalidomide and dexamethasone within its marketing authorisation for treating multiple myeloma in people who have had at least 1 previous therapy.

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 England¹. It is most frequently diagnosed in older people, with 43% of new cases in England in people aged 75 years and over¹. 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 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 129 recommends bortezomib monotherapy as an option for treating progressive multiple myeloma in people

Final scope for the appraisal of carfilzomib for previously treated multiple myeloma (part review of TA457) [ID1493]

Issue Date: August 2019

Page 1 of 6

© National Institute for Health and Care Excellence 2019. All rights reserved.

who are at first relapse and who have undergone, or are unsuitable for, bone marrow transplantation.

- 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 an anticancer drug that works by proteasome inhibition. By inhibiting proteasomes (multi-enzyme complexes present in all cells), carfilzomib disrupts the cell cycle leading to cell death. It is administered intravenously.

Carfilzomib plus lenalidomide and dexamethasone or plus dexamethasone alone has a marketing authorisation in the UK for treating adults with multiple myeloma who have had at least 1 prior therapy.

Intervention(s)	Carfilzomib plus lenalidomide and dexamethasone
Population(s)	Adults with multiple myeloma who have had at least 1 previous therapy

Comparators	<p>For people who have had 1 previous therapy:</p> <ul style="list-style-type: none"> • carfilzomib plus dexamethasone • lenalidomide plus dexamethasone • bortezomib <p>For people who have had 2 previous therapies:</p> <ul style="list-style-type: none"> • lenalidomide plus dexamethasone • panobinostat plus bortezomib and dexamethasone <p>For people who have had 3 or more previous therapies:</p> <ul style="list-style-type: none"> • lenalidomide plus dexamethasone • panobinostat plus bortezomib and dexamethasone • pomalidomide plus dexamethasone
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • 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	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.</p>
Other considerations	<p>If the evidence allows, subgroup analyses based on type and number of lines of previous therapy will be considered.</p> <p>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 in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>

<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals:</p> <p>'Lenalidomide plus dexamethasone for multiple myeloma after 1 treatment with bortezomib.' (2019) NICE technology appraisal guidance 586. Review date expected 2022.</p> <p>'Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma.' (2019) NICE technology appraisal guidance 573. Review date expected 2021.</p> <p>'Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma.' (2018) NICE technology appraisal guidance 505. Review date expected December 2019.</p> <p>'Daratumumab monotherapy for treating relapsed and refractory multiple myeloma.' (2018) NICE technology appraisal guidance 510. Review date expected November 2020.</p> <p>'Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib.' (2017) NICE technology appraisal guidance 427. (previously 338) Review date expected January 2020.</p> <p>'Carfilzomib for previously treated multiple myeloma.' (2017) NICE technology appraisal guidance 457. Review date expected July 2020.</p> <p>'Panobinostat for treating multiple myeloma after at least 2 previous treatments.' (2016). NICE Technology Appraisal 380. Review date expected January 2019.</p> <p>'Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy.' (2009). NICE Technology Appraisal 171. Guidance on static list 2014.</p> <p>'Bortezomib monotherapy for relapsed multiple myeloma.' (2007) NICE technology appraisal guidance 129. Guidance on static list 2012.</p> <p>Terminated appraisals:</p> <p>'Elotuzumab for treating relapsed or refractory multiple myeloma' NICE technology appraisal guidance [ID855]. (terminated appraisal).</p> <p>Appraisals in development (including suspended appraisals):</p> <p>'Isatuximab with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma [ID1477]'</p> <p>Elotuzumab with pomalidomide and dexamethasone for treating multiple myeloma after 2 therapies [ID1467] (suspended appraisal)</p> <p>'Pomalidomide in combination with bortezomib and dexamethasone for treating relapsed or refractory multiple</p>
--	--

	<p>myeloma' [ID1358] (suspended appraisal)</p> <p>'Plitidepsin in combination with dexamethasone for treating relapsed or refractory multiple myeloma' [ID1081] (suspended appraisal).</p> <p>Proposed technology appraisals:</p> <p>Isatuximab with carfilzomib and dexamethasone for treating relapsed or refractory multiple myeloma [ID1620]</p> <p>Related Guidelines:</p> <p>Haematological cancers: improving outcomes (2016) NICE guideline 47</p> <p>Myeloma: diagnosis and management (2016) NICE guideline 35</p> <p>Related Quality Standards:</p> <p>Haematological cancers (2017) NICE quality standard 150</p> <p>Related NICE Pathways:</p> <p>Myeloma (2017) NICE pathway</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>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]</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1,2,4,5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p> <p>Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020</p> <p>Department of Health (2014) The national cancer strategy: 4th annual report</p> <p>Department of Health (2011) Improving outcomes: a strategy for cancer</p> <p>Department of Health (2009) Cancer commissioning guidance</p> <p>Department of Health (2007) Cancer reform strategy</p>

References

¹Office of national statistics '[Cancer registration statistics, England](#)'. Accessed July 2019.

²National cancer institute '[SEER Cancer Statistics Review, 1975-2016](#)'. Accessed July 2019.

Final scope for the appraisal of carfilzomib for previously treated multiple myeloma (part review of TA457) [ID1493]

Issue Date: August 2019

Page 5 of 6

© National Institute for Health and Care Excellence 2019. All rights reserved.

³Cancer Research UK '[Myeloma survival](#)'. Accessed July 2019.