# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Appraisal

## Carfilzomib in combination with lenalidomide and dexamethasone for previously treated multiple myeloma

## Final scope

### Remit/appraisal objective

To appraise the clinical and cost effectiveness of carfilzomib in combination with lenalidomide and dexamethasone within its marketing authorisation for treating multiple myeloma in people who have received at least 1 prior 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 (due to anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems.

In 2012, 4190 people were diagnosed with multiple myeloma in England. It is most frequently diagnosed in older people, with 43% of people diagnosed aged 75 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 and Caribbean family origin. There were 2254 deaths from multiple myeloma in England in 2011.

The main aims of therapy are 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 considered suitable for people with multiple myeloma who are in good general health; however, most people with multiple myeloma are not fit enough to withstand such intensive treatments. When stem-cell transplantation is not considered suitable, NICE technology appraisal guidance 228 recommends thalidomide or bortezomib (only if the person is unable to tolerate or has contraindications to thalidomide) in combination with an alkylating agent (melphalan or cyclophosphamide) and a corticosteroid (prednisolone or dexamethasone) as initial treatment options for people with multiple myeloma.

Following initial treatment, 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 treating progressive multiple myeloma in 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 with multiple myeloma who have had at least 2 prior therapies. Other 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 (within its marketing authorisation, that is, for treating relapsed and refractory multiple myeloma in adults who have had at least 2 previous treatments, including lenalidomide and bortezomib).

## 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.

The Committee for Medicinal Products for Human Use has recommended that carfilzomib should be granted a marketing authorisation, in combination with lenalidomide and dexamethasone, for treating adults with multiple myeloma who have had at least 1 prior therapy.

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| **Intervention(s)** | Carfilzomib in combination with lenalidomide and dexamethasone |
| **Population(s)** | Adults with multiple myeloma who have received at least 1 therapy |
| **Comparators** | • bortezomib containing regimens<br>• lenalidomide in combination with dexamethasone<br>• bendamustine (not appraised by NICE but funded via the Cancer Drugs Fund)<br>• panobinostat in combination with bortezomib and dexamethasone (for people who have had at least 2 prior regimens) [subject to ongoing NICE appraisal] |

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| **Outcomes** | The outcome measures to be considered include:<br>• progression-free survival<br>• overall survival<br>• response rates (for example complete response)<br>• time to next treatment<br>• adverse effects of treatment<br>• 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.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>The availability of any patient access schemes for the intervention or comparator 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.<br>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. |
| **Related NICE recommendations and NICE Pathways** | Related Technology Appraisals:<br>Technology Appraisal No. 129, October 2007, 'Bortezomib monotherapy for relapsed multiple myeloma'. Moved to static list, November 2012.<br>Technology Appraisal No. 171, June 2009, 'Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy'. Moved to static list, November 2012.<br>Technology Appraisal No. 338, March 2015, 'Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and |

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| | bortezomib'. Review date March 2018.<br><br>Technology Appraisal in Preparation, 'Panobinostat for treating multiple myeloma after at least 2 previous treatments'. Earliest anticipated date of publication January 2016.<br><br>Suspended Technology Appraisal, 'Lenalidomide for the treatment of multiple myeloma following treatment with bortezomib' (part review of Technology Appraisal guidance 171). Date of publication TBC.<br><br>Related Guidelines:<br><br>Clinical Guideline in Preparation, 'Myeloma: diagnosis and management of myeloma'. Earliest anticipated date of publication February 2016.<br><br>Cancer Service Guidance, October 2003, 'Improving Outcomes in Haematological Cancer'.<br><br>NICE pathway:<br><br>Blood and bone marrow cancers, Pathway created: December 2013 |
| **Related National Policy** | NHS England (2014) 'Manual for prescribed specialised services 2013/14'. Chapter 29.<br><br>Department of Health (2013) 'Improving Outcomes: A Strategy for Cancer, third annual report'.<br><br>Department of Health (2014) 'NHS Outcomes Framework 2015-2016'. Domains 1, 2, 4 and 5. |