NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Carfilzomib for previously treated multiple myeloma

Draft scope

Remit/appraisal objective

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

In 2013, 4,703 people were diagnosed with multiple myeloma in England[1]. Forty-three percent of people diagnosed are 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]. The 5-year survival rate for adults with multiple myeloma in England is estimated to be 47%[2].

The main aims of therapy are to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. 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. An ongoing NICE technology appraisal is assessing lenalidomide in combination with dexamethasone for treating multiple myeloma after 1 prior treatment with bortezomib. 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. NICE technology appraisal guidance 380 recommends panobinostat in combination with bortezomib and dexamethasone as an option for treating multiple

myeloma in adult patients with relapsed and/or refractory multiple myeloma who have received at least 2 prior regimens including bortezomib and an immunomodulatory agent. For people who have had at least 3 prior therapies, treatment options include bendamustine (available through the Cancer Drugs Fund) or combination chemotherapy regimens (for example, alkylating agents such as melphalan and cyclophosphamide). 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). NICE has decided to review technology appraisal 338 because new clinical evidence is available and the company is proposing a patient access scheme for pomalidomide

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 in combination with lenalidomide and dexamethasone has a marketing authorisation in the UK for treating adults with multiple myeloma who have had at least 1 prior therapy. Carfilzomib in combination with dexamethasone does not currently have a marketing authorisation in the UK for treating multiple myeloma. It has been studied in a clinical trial in combination with dexamethasone, compared with bortezomib in combination with dexamethasone, for people with relapsed multiple myeloma who have received 1-3 prior therapies.

Intervention(s)	Carfilzomib in combination with lenalidomide and dexamethasone Carfilzomib in combination with dexamethasone
Population(s)	Adults with multiple myeloma who have received at least 1 prior therapy

Comparators	For people who have received at least 1 prior therapy: • bortezomib (with or without dexamethasone) • lenalidomide in combination with dexamethasone (subject to ongoing NICE appraisal [part review of technology appraisal 171]). For people who have received at least 2 prior therapies: • lenalidomide in combination with dexamethasone • panobinostat in combination with bortezomib and dexamethasone • pomalidomide in combination with dexamethasone (subject to ongoing NICE appraisal) • Combination chemotherapy regimens (for example, melphalan and cyclophosphamide)
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. 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.

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 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: Technology Appraisal No. 129, October 2007, 'Bortezomib monotherapy for relapsed multiple myeloma'. Guidance on static list. Technology Appraisal No. 171, June 2009, 'Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy'. Guidance on static list. Technology Appraisal No. 338, March 2015, 'Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib'. Review date March 2018. Technology Appraisal No. 380, January 2016. 'Panobinostat for treating multiple myeloma after at least 2 previous treatments' Review date January 2019. Appraisals in development: 'Lenalidomide for treating multiple myeloma after 1 prior treatment with bortezomib (part-review of TA171)' NICE technology appraisal [ID667]. Publication date to be confirmed. 'Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib (review of TA338)' NICE technology appraisal [ID985]. Publication date to be confirmed. Related Guidelines: Myeloma: diagnosis and management of myeloma' (2016). NICE guideline 35. Cancer Service Guidance, October 2003, 'Improving Outcomes in Haematological Cancer'. NICE pathway: NICE pathway: Myeloma (2016)
Related National	NHS England (2015) 'Cancer Drugs Fund list v6.1'

Policy	NHS England (2014) 'Manual for prescribed specialised services 2013/14'. Chapter 29. Department of Health (2013) 'Improving Outcomes: A Strategy for Cancer, third annual report'. Department of Health (2014) 'NHS Outcomes Framework 2015-2016'. Domains 1, 2, 4 and 5.

Questions for consultation

Is carfilzomib in combination with lenalidomide and dexamethasone and carfilzomib in combination with dexamethasone likely to be used for treating multiple myeloma after 1, 2 or 3 prior therapies in clinical practice?

For people previously treated with 1 prior therapy, specifically bortezomib (with or without dexamethasone), is retreatment with bortezomib used in clinical practice in the NHS?

For people previously treated with 2 prior therapies, specifically lenalidomide and bortezomib, is retreatment with lenalidomide used in clinical practice in the NHS?

Have all relevant comparators for carfilzomib in combination with lenalidomide and dexamethasone and carfilzomib in combination with dexamethasone been included in the scope? Which treatments are considered to be established clinical practice in the NHS for multiple myeloma following at least 1 prior therapy?

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

Where do you consider carfilzomib in combination with lenalidomide and dexamethasone and carfilzomib in combination with 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 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.

References

1. Cancer Research UK (2013). Multiple myeloma incidence statistics. Accessed February 2016.
2. Cancer Research UK (2011). Multiple myeloma survival statistics. Accessed February 2016.