NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Carfilzomib for treated multiple myeloma

Final 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.

For initial treatment:

- NICE technology appraisal guidance 311 recommends bortezomib as an option, in combination with dexamethasone or with dexamethasone and thalidomide, for the induction treatment of adults with untreated multiple myeloma who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation.

- When stem-cell transplantation is not suitable, NICE technology appraisal guidance 228 recommends thalidomide or bortezomib (only if the person is unable to tolerate or has contraindications to thalidomide) as an option, in combination with an alkylating agent (melphalan or cyclophosphamide) and a corticosteroid (prednisolone or dexamethasone).

Following 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.

- An ongoing NICE technology appraisal is assessing lenalidomide for treating multiple myeloma after 1 prior treatment with bortezomib.

For people who have had at least 2 prior therapies:

- NICE technology appraisal guidance 171 recommends lenalidomide in combination with dexamethasone as a treatment option.

- NICE technology appraisal guidance 380 recommends panobinostat in combination with bortezomib and dexamethasone as a treatment option for people with relapsed and refractory multiple myeloma who have received at least 2 prior therapies 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 conventional chemotherapy regimens (for example, alkylating agents such as melphalan and cyclophosphamide).

NICE technology appraisal guidance 338 does not recommend pomalidomide within its marketing authorisation for treating relapsed and refractory multiple myeloma. 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) For people who have received at least 3 prior therapies: • panobinostat in combination with bortezomib and dexamethasone • pomalidomide in combination with dexamethasone (subject to ongoing NICE appraisal) • bendamustine (not appraised by NICE but funded via the Cancer Drugs Fund; does not currently have a marketing authorisation in the UK for this indication) • Conventional chemotherapy regimens (including but not limited to 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. Expected date of publication April 2017 'Ixazomib citrate in combination with lenalidomide and dexamethasone for relapsed or refractory multiple myeloma'. NICE technology appraisal ID807. Expected publication date January 2017 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 Policy	NHS England (2015) 'Cancer Drugs Fund list v6.1' 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.

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.