NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Carfilzomib for treating multiple myeloma in people who have received at least 1 prior therapy

Draft scope (pre-referral)

Draft 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 supress 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 in England in 2011. The 5-year survival rate for adults with multiple myeloma in England is estimated to be 42.2%.

Multiple myeloma is an incurable disease. 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 in good general health. 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, cyclophosphamide) and a corticosteroid (prednisolone, 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 received 1 prior therapy and who have undergone, or are unsuitable for bone marrow transplantation. NICE technology appraisal guidance 171 also recommends lenalidomide in combination with dexamethasone as a treatment option for people with multiple myeloma who have received at least 2 prior therapies. Other subsequent treatment options may include repeating high-dose chemotherapy or chemotherapy with alkylating agents and anthracyclines, thalidomide and corticosteroids.

The technology

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

Carfilzomib does not currently have a marketing authorisation in the UK for treating multiple myeloma following at least 1 prior therapy. It has been studied in clinical trials in combination with lenalidomide and dexamethasone, compared with lenalidomide 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
Population(s)	People with multiple myeloma who have received at least 1 prior therapy.
Comparators	• bortezomib, alone or in combination with dexamethasone • lenalidomide, in combination with dexamethasone • thalidomide containing regimens • pomalidomide, in combination with dexamethasone (subject to NICE guidance and currently in the Cancer Drugs Fund) • chemotherapy including regimens based on melphalan, vincristine, cyclophosphamide or doxorubicin • bendamustine

Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rates • 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 should be taken into account. Where comparator technologies are available through the Cancer Drugs Fund, the cost incurred by the Cancer Drugs Fund should be used in any economic analyses, rather than the list price.
Other considerations	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. If the evidence allows, subgroup analyses based on type and number of lines of previous therapy will be considered.
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 in Preparation, 'Panobinostat for treating relapsed and refractory multiple myeloma previously treated with bortezomib'. Earliest anticipated date of publication January 2016. Technology Appraisal in Preparation, 'Pomalidomide for treating relapsed and refractory multiple myeloma previously treated with both lenalidomide and bortezomib'. Earliest anticipated date of publication February 2015. Technology Appraisal in Preparation, 'Lenalidomide for the treatment of multiple myeloma following treatment with bortezomib' (part review of Technology Appraisal guidance 171). Earliest anticipated date of publication TBC. Related Guidelines: Clinical Guideline in Preparation, 'Multiple myeloma: diagnosis and management of multiple myeloma'. Earliest anticipated date of publication January 2016. Cancer Service Guidance, October 2003, 'Improving Outcomes in Haematological Cancer'. NICE pathway: Blood and bone marrow cancers, Pathway created: December 2013 http://pathways.nice.org.uk/
Related National Policy	NHS England, Manual for prescribed specialised services 2013/14. Chapter 29. http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf Department of Health, Improving Outcomes: A Strategy for Cancer, third annual report, Dec 2013 https://www.gov.uk/government/publications/the-national-cancer-strategy-3rd-annual-report--2 Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf Department of Health, Cancer commissioning guidance, Dec 2009. http://webarchive.nationalarchives.gov.uk/20130107105354/http:/www.dh.gov.uk/en/Publicationsandstatistics/Pu

	blications/PublicationsPolicyAndGuidance/DH_110115

Questions for consultation

Have all relevant comparators for carfilzomib in combination with lenalidomide and 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 is 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 will fit into the existing NICE pathway, blood and bone marrow cancers?

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.

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)