NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Panobinostat for treating relapsed and refractory multiple myeloma previously treated with bortezomib

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of panobinostat within its licensed indication for treating relapsed and refractory multiple myeloma previously treated with bortezomib.

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 2010, 3941 people were diagnosed with multiple myeloma in England. It is most frequently diagnosed in older people, with 71% of people diagnosed aged 65 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 37.1%.

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. People with multiple myeloma in good general health may be considered suitable for high dose chemotherapy with autologous stem cell transplantation. For people with multiple myeloma not considered suitable for stem-cell transplantation, NICE technology appraisal guidance 228 recommends a range of first-line treatment options including thalidomide or bortezomib (only if person is unable to tolerate or has contraindications to thalidomide), alkylating agents (melphalan, cyclophosphamide) and corticosteroids (prednisolone, dexamethasone).

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

Panobinostat (brand name unknown, Novartis) is an oral potent histone deacetylase inhibitor that disrupts a key mechanism in the transformation of normal cells to cancerous cells and selectively targets tumour cells for cell death.

Panobinostat does not currently have a UK marketing authorisation for treating relapsed and refractory multiple myeloma previously treated with bortezomib. Panobinostat has been studied in combination with bortezomib and dexamethasone compared with bortezomib and dexamethasone in adults with relapsed and refractory multiple myeloma.

Intervention(s)	Panobinostat (in combination with bortezomib and dexamethasone)
Population(s)	People with relapsed and refractory multiple myeloma previously treated with bortezomib
Comparators	Established clinical management without panobinostat
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rates • 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.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
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. Part review of Technology Appraisal No. 171 in Preparation, 'Lenalidomide for the treatment of multiple myeloma following treatment with bortezomib'. Earliest anticipated date of publication July 2014. 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. 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: Multiple myeloma, Pathway created: December 2013 http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers#path=view%3A/pathways/blood-and-

	bone-marrow-cancers/multiple-myeloma.xml&content=close
Related NHS England Policy	National service framework: 'Improving outcomes: a strategy for cancer', January 2011. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/135516/dh_123394.pdf.pdf

Questions for consultation

Will panobinostat be given as an add-on therapy with bortezomib and dexamethasone or is it likely to be given as a monotherapy in UK clinical practice?

Have all relevant comparators for panobinostat been included in the scope? Which treatments are considered to be established clinical practice in the NHS for relapsed and refractory multiple myeloma previously treated with bortezomib?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider panobonistat will fit into the NICE pathway, Multiple 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 panobinostat 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 the technology 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 the technology 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/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)