NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Proposed Health Technology Appraisal

Ixazomib citrate in combination with lenalidomide and dexamethasone for relapsed or refractory multiple myeloma

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ixazomib citrate within its marketing authorisation for relapsed or refractory multiple myeloma.

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[1]. It is most frequently diagnosed in older people, with 57%[2] of people diagnosed aged 75 years and over between 2010 and 2012. 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 2303[3] deaths in England in 2012. The 5-year survival rate for adults with multiple myeloma in England is estimated to be 42.8%[4].

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. 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. However, lenalidomide is available through the Cancer Drugs Fund for people with multiple myeloma who have received 1 previous therapy. Other subsequent treatment options may include repeating high-dose

chemotherapy or chemotherapy with alkylating agents and anthracyclines, thalidomide and corticosteroids.

The technology

Ixazomib citrate (brand name unknown, Takeda UK) is an oral small molecule, proteasome inhibitor, which acts by inducing apoptosis via the disruption of proliferative tumour cells.

Ixazomib citrate does not currently have a marketing authorisation in the UK for previously treated relapsed or refractory multiple myeloma. Ixazomib citrate has been studied in combination with lenalidomide and dexamethasone in a randomised controlled trial compared with placebo plus lenalidomide and dexamethasone in adults with relapsed and or refractory multiple myeloma.

Intervention(s)	Ixazomib in combination with lenalidomide and dexamethasone
Population(s)	People with relapsed or refractory multiple myeloma who have received at least 1 therapy
Comparators	• bortezomib (with or without dexamethasone) • lenalidomide with dexamethasone • panobinostat with bortezomib and dexamethasone (subject to ongoing NICE appraisal)
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.
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 only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. If the evidence allows, subgroup analyses based on number of lines of previous therapy will be considered.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Bortezomib monotherapy for relapsed multiple myeloma (2007) NICE Technology Appraisal 129. Guidance on Static list. Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy (2009) NICE Technology Appraisal 171. Guidance on Static list. Appraisals in development (including suspended appraisals): Technology Appraisal in Preparation, 'Multiple myeloma (relapsed, refractory) - carfilzomib (after prior therapy)' NICE technology appraisal [ID677]. Earliest anticipated date of publication TBC Technology Appraisal in Preparation, 'Panobinostat for treating multiple myeloma in people who have received at least one prior therapy' NICE Technology Appraisal [ID663]. Earliest anticipated date of publication January 2016. Suspended appraisal, 'Lenalidomide for the treatment of multiple myeloma following treatment with bortezomib' (part review of Technology Appraisal guidance 171)

	NICE Technology Appraisal [ID667]. Earliest anticipated date of publication TBC. Related Guidelines: Clinical Guideline in Preparation, 'Myeloma: diagnosis and management of myeloma'. Earliest anticipated date of publication February 2016. Cancer Service Guidance, October 2003, 'Improving Outcomes in Haematological Cancer'. Next review date September 2019. 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 National Policy	National service framework: 'Improving outcomes: a strategy for cancer', December 2014 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/388160/fourth_annual_report.pdf Department of Health, NHS Outcomes Framework 2015-2016, Nov 2014. Domains 1, 2, 4 and 5. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf

Questions for consultation

Have all relevant comparators for ixazomib citrate been included in the scope?

- Would panobinostat plus bortezomib and dexamethasone be a relevant comparator?
- Which treatments are considered to be established clinical practice in the NHS for relapsed and refractory multiple myeloma?

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

Where do you consider ixazomib citrate will fit into the existing 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 ixazomib citrate 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 ixazomib citrate 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 ixazomib citrate 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)

References

1. Stats updated to 2012 (ONS) http://www.ons.gov.uk/ons/rel/vsob1/cancer-statistics-registrations--england--series-mb1-/no--43--2012/rft-cancer-registration-statistics.xls [accessed July 2015]

2. http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/myeloma/mortality#heading-One [accessed July 2015]

3. http://www.cancerresearchuk.org/cancer-info/cancerstats/types/myeloma/mortality/) [accessed July 2015]

4. http://www.ons.gov.uk/ons/rel/cancer-unit/cancer-survival/cancer-survival-in-england--patients-diagnosed-2007-2011-and-followed-up-to-2012/rft-patients-diagnosed-2007-2011-and-followed-up-to-2012.xls [accessed July 2015]