NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Ixazomib with lenalidomide and dexamethasone for untreated multiple myeloma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of ixazomib in combination with lenalidomide and dexamethasone within its marketing authorisation for untreated multiple myeloma in people for whom a stem cell transplant is unsuitable.

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 2016, 4,731 people were diagnosed with multiple myeloma in England[1]. It is most frequently diagnosed in older people, with 44% of people diagnosed aged 75 years and over in 2016[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]. There were 2,769 deaths in England and Wales in 2016[2]. The 5-year survival rate for adults with multiple myeloma in England is estimated to be 51%[3].

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 an option for people with multiple myeloma in good general health; however, this is an intensive treatment, which is not considered appropriate for most people with multiple myeloma.

NICE technology appraisal guidance 228 recommends thalidomide in combination with an alkylating agent and a corticosteroid for the first-line treatment of multiple myeloma in people for whom high-dose chemotherapy with stem cell transplantation is considered inappropriate. If the person is unable to tolerate or has contraindications to thalidomide, NICE technology

appraisal guidance 228 recommends bortezomib in combination with an alkylating agent and a corticosteroid.

The technology

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

Ixazomib does not currently have a marketing authorisation in the UK for untreated multiple myeloma. It has been studied in combination with lenalidomide and dexamethasone compared with placebo plus lenalidomide and dexamethasone in people with untreated multiple myeloma for whom a stem cell transplant is unsuitable.

Intervention(s)	Ixazomib in combination with lenalidomide and dexamethasone
Population(s)	People with untreated multiple myeloma for whom a stem cell transplant is unsuitable
Comparators	• thalidomide in combination with an alkylating agent and a corticosteroid • lenalidomide in combination with dexamethasone (subject to ongoing NICE appraisal) For people who are unable to tolerate, or have contraindications to thalidomide: • bortezomib in combination with an alkylating agent and a corticosteroid
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 will 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.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** Bortezomib and thalidomide for the first-line treatment of multiple myeloma (2011) NICE technology appraisal guidance 228. Transferred to static list April 2015 **Technology Appraisals in development (including suspended appraisals):** Lenalidomide for previously untreated multiple myeloma. NICE technology appraisal guidance ID474. Appraisal suspended, publication date: TBC **Proposed Technology Appraisals:** Elotuzumab for multiple myeloma. Proposed NICE technology appraisal ID966, publication date: TBC Daratumumab with lenalidomide and dexamethasone for untreated multiple myeloma. Proposed NICE technology appraisal ID1352, publication: TBC **Related Guidelines:** Myeloma: diagnosis and management (2016) NICE guideline 35. Review date 2018 **Related NICE Pathways:** Multiple myeloma (2013) NICE Pathway
Related National Policy	NHS England Manual for prescribed specialised services 2017/2017. Blood and marrow transplantation services (adults and children) [section 29, page 79-80]:

	https://www.england.nhs.uk/wp-content/uploads/2017/10/prescribed-specialised-services-manual-2.pdf 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 2016-2017 (published 2016): Domains 1, 2, 4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for ixazomib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for untreated multiple myeloma when a stem cell transplant is unsuitable?

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

Where do you consider ixazomib 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 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 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 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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. ONS (2018) Cancer Registration Statistics, England 2016: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancerregistrationstatisticscancerregistrationstatisticsengland [Accessed March 2018]

2. ONS (2017) Death registrations summary tables - England and Wales 2016: https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/deathregistrationssummarytablesenglandandwalesreferencetables [Accessed March 2018]

3. ONS (2017) Cancer survival in England - adults diagnosed 2011-2015: https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/datasets/cancersurvivalratescancersurvivalinenglandadultsdiagnosed [Accessed March 2018]