

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Final scope

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 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 (due to anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems.

In 2013, about 4,700 people were diagnosed with multiple myeloma in England.¹ It is most frequently diagnosed in older people, with 59% of people diagnosed aged 70 years and over.² 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. The 5-year survival rate for adults with multiple myeloma in England and Wales is estimated to be 47%.³

The main aims of therapy are to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. Initial therapy can include induction treatment with bortezomib (given with dexamethasone, or with dexamethasone and thalidomide) before having chemotherapy and stem cell transplantation (NICE technology appraisal 311). If high-dose chemotherapy with stem cell transplantation is inappropriate, NICE technology appraisal guidance 228 recommends thalidomide (or bortezomib if the person is unable to tolerate or has contraindications to thalidomide) in combination with an alkylating agent and a corticosteroid.

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

recommends lenalidomide in combination with dexamethasone as a treatment option for people with multiple myeloma who have received at least 2 prior therapies. NICE technology appraisal guidance 380 recommends panobinostat in combination with bortezomib and dexamethasone as an option for treating relapsed and/or refractory multiple myeloma in adults who have had at least 2 prior regimens including bortezomib and an immunomodulatory agent. Other subsequent treatment options may include repeating high-dose chemotherapy or chemotherapy with alkylating agents and anthracyclines, thalidomide and corticosteroids.

The technology

Ixazomib citrate (Ninlaro, 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 treating multiple myeloma. A randomised controlled trial compared ixazomib citrate with placebo, both in combination with lenalidomide and dexamethasone, in adults with relapsed or refractory multiple myeloma.

Intervention	Ixazomib in combination with lenalidomide and dexamethasone
Population	People with relapsed or refractory multiple myeloma who have had at least 1 therapy
Comparators	<p>For people who have had at least 1 therapy:</p> <ul style="list-style-type: none"> • bortezomib (with or without dexamethasone)* • bortezomib retreatment (with or without dexamethasone) • lenalidomide with dexamethasone (subject to ongoing NICE appraisal [part review of technology appraisal 171]) <p>For people who have had at least 2 therapies:</p> <ul style="list-style-type: none"> • lenalidomide with dexamethasone • panobinostat with bortezomib and dexamethasone

* NICE recommends bortezomib monotherapy as an option for treating multiple myeloma at first relapse. In clinical practice, bortezomib is often given in combination with dexamethasone.

Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> • progression-free survival • overall survival • response rates • time to next treatment • adverse effects of treatment • health-related quality of life.
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies should be taken into account.</p>
Other considerations	<p>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.</p> <p>If the evidence allows, subgroup analyses based on number of lines of previous therapy will be considered.</p>
Related NICE recommendations and NICE Pathways	<p>Related Technology Appraisals:</p> <p>Bortezomib monotherapy for relapsed multiple myeloma (2007) NICE technology appraisal 129. Guidance on static list.</p> <p>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.</p> <p>Panobinostat for treating multiple myeloma in people who have received at least one prior therapy (2016) NICE technology appraisal 380. Review date January 2019.</p>

	<p>Appraisals in development:</p> <p>Carfilzomib in combination with dexamethasone for treating multiple myeloma in people who have received at least 1 prior therapy. NICE technology appraisal ID934. Date of publication TBC.</p> <p>Elotuzumab for previously treated multiple myeloma. NICE technology appraisal ID855. Date of publication TBC.</p> <p>Lenalidomide for treating multiple myeloma after 1 prior treatment with bortezomib (part review of Technology Appraisal guidance 171). NICE technology appraisal ID667. Date of publication TBC.</p> <p>Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib (review of TA338). NICE technology appraisal ID985. Date of publication April 2017.</p> <p>Suspended appraisal, Carfilzomib in combination with lenalidomide and dexamethasone for previously treated multiple myeloma. NICE technology appraisal ID677.</p> <p>Suspended appraisal, Lenalidomide for treating newly diagnosed multiple myeloma. NICE technology appraisal ID747.</p> <p>Related Guidelines:</p> <p>NICE Guideline 35, Myeloma: diagnosis and management of myeloma. February 2016.</p> <p>NICE pathway:</p> <p>Multiple myeloma: http://pathways.nice.org.uk/pathways/myeloma</p>
<p>Related National Policy</p>	<p>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</p> <p>NHS England Manual for prescribed specialised services 2013/2014. Blood and marrow transplantation services (all ages) https://www.england.nhs.uk/commissioning/spec-services/npc-crg/blood-and-infection-group-f/f01/</p> <p>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</p>

References

1. Cancer research UK, [Myeloma incidence statistics](#) [accessed March 2016]
2. Cancer research UK, [Myeloma survival statistics](#) [accessed March 2016]