

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (CDF review of TA505) [ID1635]

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.

Between 2015 and 2017, 5,820 people were diagnosed with multiple myeloma in England. It is most frequently diagnosed in older people, over the incident rates are highest in people aged 85 to 89 years old. ¹ 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 52.3%.²

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. NICE technology appraisal guidance 587 recommends lenalidomide plus dexamethasone for previously untreated multiple myeloma in adults who are not eligible for a stem cell transplant, only if: thalidomide is contraindicated, and the person cannot tolerate thalidomide.

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 586 recommends lenalidomide with dexamethasone for multiple myeloma as an option for adults who have had one previous therapy with bortezomib, and the company can provide it according to the commercial arrangement. 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 in combination with lenalidomide and dexamethasone has a marketing authorisation in the UK for the treatment of multiple myeloma in adults who have received at least one prior therapy.

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 <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

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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will 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 2 prior therapies’ (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</p>

	<p>2021.</p> <p>‘Carfilzomib for previously treated multiple myeloma’ (2020) NICE technology appraisal 657. Review date November 2023.</p> <p>‘Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma’ (2020) NICE technology appraisal 658. Review date November 2022.</p> <p>‘Lenalidomide plus dexamethasone for multiple myeloma after 1 treatment with bortezomib’ (2019) NICE technology appraisal 586. Review date June 2022</p> <p>‘Lenalidomide plus dexamethasone for previously untreated multiple myeloma’ (2019) NICE technology appraisal 587. Review date June 2022</p> <p>‘Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma’ (2019) NICE technology appraisal 573. Review date April 2021.</p> <p>‘Daratumumab monotherapy for treating relapsed and refractory multiple myeloma’ (2018) NICE technology appraisal 510. Review date to be confirmed.</p> <p>‘Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib’ (2017) NICE technology appraisal 427. Review date to be confirmed.</p> <p>‘Panobinostat for treating multiple myeloma after at least 2 previous treatments’ (2016) NICE technology appraisal 380. Review date to be confirmed.</p> <p>Terminated appraisals:</p> <p>Pomalidomide with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2019) NICE technology appraisal guidance 602.</p> <p>Bortezomib for treating multiple myeloma after second or subsequent relapse (terminated appraisal) (2017) NICE technology appraisal guidance 453.</p> <p>Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2017) NICE technology appraisal guidance 454.</p> <p>Elotuzumab for previously treated multiple myeloma (terminated appraisal) (2017) NICE technology appraisal guidance 434.</p> <p>Appraisals in development (including suspended</p>
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appraisals):

[‘Belantamab mafodotin for treating relapsed or refractory multiple myeloma after 3 therapies’](#) NICE technology appraisal ID 2701. Publication date to be confirmed.

[‘Carfilzomib with daratumumab and dexamethasone for treating relapsed or refractory multiple myeloma’](#) NICE technology appraisal ID 2709. Publication date to be confirmed.

[‘Carfilzomib with dexamethasone and lenalidomide for treating multiple myeloma after at least 1 previous therapy’](#) NICE technology appraisal ID 1493. Publication date to be confirmed.

[‘Ciltacabtagene autoleucl for treating relapsed or refractory multiple myeloma’](#) NICE technology appraisal ID 3816. Publication date to be confirmed.

[‘Daratumumab with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma’](#) NICE technology appraisal ID 3775. Suspended.

[‘Elotuzumab with pomalidomide and dexamethasone for treating multiple myeloma after 2 therapies’](#) NICE technology appraisal ID1467. Suspended.

[‘Idecabtagene vicleucl for treating relapsed and refractory multiple myeloma in people who have received at least 3 prior therapies’](#) NICE technology appraisal ID 1442. Publication date to be confirmed.

[‘Isatuximab with carfilzomib and dexamethasone for treating relapsed or refractory multiple myeloma’](#) NICE technology appraisal ID1620. Suspended.

[‘Melphalan flufenamide with dexamethasone for treating relapsed or refractory multiple myeloma’](#) NICE technology appraisal ID 3862. Publication date to be confirmed.

[‘Multiple myeloma \(one prior therapy\) - vorinostat \(with bortezomib\)’](#) NICE technology appraisal ID 501. Suspended.

[‘Pelareorep for treating relapsed or refractory multiple myeloma’](#) NICE technology appraisal ID1028. Suspended.

[‘Pembrolizumab for previously treated multiple myeloma’](#) NICE technology appraisal ID1139. Suspended.

[‘Plitidepsin in combination with dexamethasone for treating relapsed or refractory multiple myeloma’](#) NICE

	<p>technology appraisal ID1081. Suspended.</p> <p>‘Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma’ NICE technology appraisal ID3797. Publication date to be confirmed.</p> <p>‘Selinexor with low-dose dexamethasone for treating refractory multiple myeloma’ NICE technology appraisal ID1535. Publication date to be confirmed.</p> <p>Related Guidelines:</p> <p>NICE Guideline 35, Myeloma: diagnosis and management of myeloma. February 2016.</p> <p>NICE Guideline 47, Haematological cancers: improving outcomes. May 2016</p> <p>Related Quality Standards:</p> <p>Haematological cancers (2017) NICE quality standard 150</p> <p>Related NICE Pathways:</p> <p>Myeloma (2017) NICE pathway</p>
<p>Related National Policy</p>	<p>The NHS Long Term Plan, 2019. NHS Long Term Plan</p> <p>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Blood and marrow transplantation services (adults and children) [section 29, pages 98-100]</p> <p>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</p>

References

1. Cancer research UK, [Myeloma incidence statistics](#) [accessed February 2021]
2. Cancer research UK, [Myeloma survival statistics](#) [accessed February 2021]