NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy with bortezomib (partial review of TA171)

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of lenalidomide within its licensed indication for treating multiple myeloma previously treated with bortezomib[1] [2].

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

In 2009, 4270 people were diagnosed with multiple myeloma in England and Wales. The condition 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. 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. For people with multiple myeloma who are not considered suitable for stem-cell transplantation, NICE TA228 recommends as a first line treatment option thalidomide given with alkylating agents (such as melphalan or cyclophosphamide) and corticosteroids (such as prednisolone or dexamethasone) or, if thalidomide is contraindicated, bortezomib given with alkylating agents and corticosteroids. TA129 recommends bortezomib monotherapy as a second line treatment option for

[1] This is a part-review of TA171 (the rest of the appraisal will be placed on the static list).
[2] The remit for TA171 was: 'To appraise the clinical and cost effectiveness of lenalidomide in combination with dexamethasone for the treatment of multiple myeloma in people who have received at least one prior therapy'.

the treatment of progressive multiple myeloma in people who are at first relapse having received one prior therapy and who have undergone, or are unsuitable for, bone marrow transplantation (if the response to bortezomib is measured using serum M protein after a maximum of four cycles of treatment, and treatment is continued only in people who have a complete or partial response). TA171 recommends lenalidomide in combination with dexamethasone as a third line treamtent option for the treatment of multiple myeloma only in people who have received two or more prior therapies.

First-line treatment of multiple myeloma with bortezomib was not an option during the development of TA171. Therefore, recommendations on the treatment of multiple myeloma with lenalidomide in people for whom thalidomide is contraindicated and who have received first-line line treatment with bortezomib are being developed in the current part-review.

The technology

Lenalidomide (Revlimid, Celgene) is a structural analogue of thalidomide. It has anti-neoplastic, anti-angiogenic, pro-erythropoeitic, anti-inflammatory and immunomodulatory properties. Lenalidomide is administered orally.

Lenalidomide in combination with dexamethasone has a UK marketing authorisation for the treatment of multiple myeloma in adults who have received at least one prior therapy.

Intervention(s)	Lenalidomide in combination with dexamethasone.
Population(s)	Adults with multiple myeloma for whom thalidomide is contraindicated and whose disease has progressed after at least 1 prior treatment with bortezomib.
Comparators	• Bortezomib monotherapy and bortezomib in combination with high dose dexamethasone • Chemotherapy including regimens based on mephalan, vincristine, cyclophosphamide and doxorubicin • Bendamustine
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.

Related NICE recommendations and NICE pathways	Related Technology Appraisals: Technology Appraisal No. 129, October 2007, 'Bortezomib monotherapy for relapsed multiple myeloma'. 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'. Static list. Technology Appraisal No. 228, July 2011, 'Bortezomib and thalidomide for the first-line treatment of multiple myeloma'. Review proposal date July 2014. Suspended Technology Appraisal 'Multiple myeloma - lenalidomide (maintenance, post autologous stem cell transplantation)'. Suspended Technology Appraisal, 'Vorinostat in combination with bortezomib for the treatment of multiple myeloma in people who have received at least one prior therapy'. Suspended Technology Appraisal, 'Lenalidomide for the treatment of newly diagnosed multiple myeloma' 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'.
Related NHS England policy	National service framework: 'Improving outcomes: a strategy for cancer', Jan 2011. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/135516/dh_123394.pdf.pdf

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Single Technology Appraisal

Lenalidomide for the treatment of multiple myeloma in people who have received at least one prior therapy with bortezomib (partial review of TA171)

Final matrix of consultees and commentators

Consultees	**Commentators (no right to submit or appeal)**
Manufacturers/sponsors • Celgene (lenalidomide) Patient/carer groups • Afiya Trust • Black Health Agency • Cancer 52 • Cancer Black Care • Cancer Equality • Equalities National Council • Helen Rollason Cancer Charity • Independent Age • Independent Cancer Patients Voice • Leukaemia Cancer Society • Leukaemia CARE • Macmillan Cancer Support • Maggie's Centres • Marie Curie Cancer Care • Muslim Council of Britain • Muslim Health Network • Myeloma UK • Rarer Cancers Foundation • South Asian Health Foundation • Specialised Healthcare Alliance • Tenovus Professional groups • Association of Cancer Physicians • British Association for Services to the Elderly • British Committee for Standards in Haematology • British Geriatrics Society • British Psychosocial Oncology Society • British Society of Haematology • Cancer Network Pharmacists Forum • Cancer Research UK • Royal College of General Practitioners • Royal College of Nursing • Royal College of Pathologists • Royal College of Physicians	General • Allied Health Professionals Federation • Board of Community Health Councils in Wales • British National Formulary • Care Quality Commission • Commissioning Support Appraisals Service • Department of Health, Social Services and Public Safety for Northern Ireland • Healthcare Improvement Scotland • Medicines and Healthcare products Regulatory Agency • National Association of Primary Care • National Pharmacy Association • NHS Alliance • NHS Commercial Medicines Unit • NHS Confederation • Public Health England • Public Health Wales NHS Trust • Scottish Medicines Consortium Comparator manufacturers • Accord (doxorubicin) • Actavis (doxorubicin) • Aspen (melphalan) • Baxter Healthcare (cyclophosphamide) • Genus Pharmaceuticals (vincristine) • Hameln Pharmaceuticals (dexamethasone) • Hospira UK (dexamethasone, doxorubicin, vincristine) • Janssen-Cilag (bortezomib) • Medac GmbH (doxorubicin) • Merck, Sharp and Dohme (dexamethasone) • Napp Pharmaceuticals (bendamustine) • Pfizer (cyclophosphamide, doxorubicin,) • Rosemount Pharmaceuticals (dexamethasone) • Teva UK (vincristine) • Wockhardt UK (doxorubicin) Relevant research groups

Consultees	Commentators (no right to submit or appeal)
• Royal College of Radiologists • Royal Pharmaceutical Society • Royal Society of Medicine • UK Health Forum • UK Myeloma Forum • United Kingdom Clinical Pharmacy Association • United Kingdom Oncology Nursing Society <u>Others</u> • Department of Health • NHS England • NHS Leeds South and East CCG • NHS Telford & Wrekin CCG • Welsh Government	• Cochrane Haematological Malignancies Group • Elimination of Leukaemia Fund • Health Research Authority • Leukaemia and Lymphoma Research • Institute of Cancer Research • MRC Clinical Trials Unit • National Cancer Research Institute • National Cancer Research Network • National Institute for Health Research • Research Institute of the Care of Older People <u>Assessment Group</u> • National Institute for Health Research Health Technology Assessment Programme • TBC <u>Associated Guideline Groups</u> • National Collaborating Centre for Cancer <u>Associated Public Health Groups</u> • None

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people who share a protected characteristic and those who do not. Please let us know if we have missed any important organisations from the lists in the matrix, and which organisations we should include that have a particular focus on relevant equality issues.

PTO for definitions of commentators and consultees

Definitions:

Consultees
Organisations that accept an invitation to participate in the appraisal; the manufacturer(s) or sponsor(s) of the technology; national professional organisations; national patient organisations; the Department of Health and the Welsh Government and relevant NHS organisations in England.

The manufacturer/sponsor of the technology is invited to make an evidence submission, respond to consultations and has the right to appeal against the Final Appraisal Determination (FAD).

All non-manufacturer/sponsor consultees are invited to submit a statement[1], respond to consultations, nominate clinical specialists or patient experts and have the right to appeal against the Final Appraisal Determination (FAD).

Commentators

Organisations that engage in the appraisal process but that are not asked to prepare an evidence submission or statement, are able to respond to consultations and they receive the FAD for information only, without right of appeal. These organisations are: manufacturers of comparator technologies; NHS Quality Improvement Scotland; the relevant National Collaborating Centre (a group commissioned by the Institute to develop clinical guidelines); other related research groups where appropriate (for example, the Medical Research Council [MRC], National Cancer Research Institute); other groups (for example, the NHS Confederation, NHS Alliance and NHS Commercial Medicines Unit, and the British National Formulary.

All non-manufacturers/sponsors commentators are invited to nominate clinical specialists or patient experts.

Assessment Group

An independent academic group (commissioned by the National Institute for Health Research (NIHR) Health Technology Assessment Programme (HTA Programme) to assist in the appraisal) prepares an Assessment Report on the health technology (a review of the clinical and cost effectiveness of the technology(ies) based on a systematic review of the literature and a review of manufacturer and sponsor submission to the Institute).

[1] Non manufacturer consultees are invited to submit statements relevant to the group they are representing.