Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Lenalidomide in combination with dexamethasone for previously untreated multiple myeloma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of lenalidomide in combination with dexamethasone within its marketing authorisation for previously untreated multiple myeloma in people for whom stem-cell transplantation is considered inappropriate.

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 2014, 5,501 people were diagnosed with multiple myeloma in England[i]. Fifty-nine percent of people diagnosed in the UK are aged 70 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 family origin[ii]. The 5-year survival rate for adults with multiple myeloma in England and Wales is about 47%[iii].

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

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

Lenalidomide as combination therapy (with dexamethasone) has a marketing authorisation in the UK for treating 'adult patients with previously untreated multiple myeloma who are not eligible for transplant' until disease progression. It is also has marketing authorisation as monotherapy for treating 'adult patients with newly diagnosed multiple myeloma who have undergone autologous stem cell transplantation' (subject to a separate ongoing NICE appraisal[1]), and in combination with dexamethasone for treating 'adult patients who have received at least one prior therapy'.

Intervention	Lenalidomide in combination with dexamethasone
Population	Adults with previously untreated multiple myeloma for whom stem-cell transplantation is considered inappropriate
Comparators	• Thalidomide in combination with an alkylating agent and a corticosteroid For people who are unable to tolerate, or have contraindications to thalidomide: • Bortezomib in combination with an alkylating agent and a corticosteroid

[1] Lenalidomide as maintenance treatment of multiple myeloma after autologous stem cell transplantation [ID475]: see https://www.nice.org.uk/guidance/indevelopment/gid-tag430

Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • time to next treatment • time to treatment failure • 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	**Related Technology Appraisals:** Bortezomib and thalidomide for the first line treatment of multiple myeloma (2011). NICE Technology Appraisal 228. Static list. **Related Guidelines:** 'Myeloma: diagnosis and management of myeloma' (2016). NICE guideline 35. Review date to be confirmed. 'Haematological cancers – improving outcomes' (2016) NICE guideline 47 Review date to be confirmed. **Related NICE Pathways:** Blood and bone marrow cancers http://pathways.nice.org.uk/pathways/blood-and-bone-

	marrow-cancers
Related National Policy	NHS England Manual for prescribed specialised services 2016/2017. Blood and marrow transplantation services (adults and children) [section 29, page 80-82]: https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf Department of Health, NHS Outcomes Framework 2016-2017, April 2016. Domains 1–5: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/513157/NHSOF_at_a_glance.pdf

References

[i] Cancer Research UK 'Myeloma incidence by sex and UK region'. Accessed December 2016.

[ii] Cancer Research UK 'Myeloma incidence'. Accessed December 2016.

[iii] Cancer Research UK 'Myeloma survival'. Accessed December 2016.