NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma [Review of TA658]

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of isatuximab within its marketing authorisation for treating relapsed and 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 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 (due to anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems.

Approximately 5,000 people are diagnosed with multiple myeloma in England each year (2016 to 2018 data)[1]. Five-year prevalence of multiple myeloma in the UK is 26 per 100,000[2]. It is most frequently diagnosed in older people, with 43% of new cases of multiple myeloma in England in people aged 75 years or older[1]. The 5-year survival rate for adults with multiple myeloma in England and Wales is estimated to be 52%[3]. Multiple myeloma is more common in men than in women[4]. The incidence rates are also reported to be lower in the Asian ethnic group, higher in the Black ethnic group, and similar in people of mixed or multiple ethnicity, compared with the White ethnic group, in England (2013-2017 data)[4].

The main aims of therapy are to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. If the disease progresses after initial treatment, the choice of subsequent therapy is influenced by previous treatment and response to it, duration of remission, comorbidities and patient preference.

For people who have had at least 2 prior therapies:

- NICE technology appraisal guidance 171 recommends lenalidomide plus dexamethasone as a treatment option for people with multiple myeloma who have had at least 2 prior therapies.

- NICE technology appraisal guidance 380 recommends panobinostat plus bortezomib and dexamethasone as a treatment option for adults who have had at least 2 prior therapies including bortezomib and an immunomodulatory agent.

- NICE technology appraisal guidance 505 recommends ixazomib citrate plus lenalidomide and dexamethasone for use within the Cancer Drugs Fund as a treatment option for adults who have had 2 or 3 previous therapies.

For people who have had at least 3 prior therapies:

- NICE technology appraisal guidance 427 recommends pomalidomide plus low-dose dexamethasone as a treatment option for adults who have had at least 3 previous treatments including both lenalidomide and bortezomib.

- NICE technology appraisal guidance 783 recommends daratumumab monotherapy for use as a treatment option for adults who have had 3 previous treatments including a proteasome inhibitor and an immunomodulator.

- NICE technology appraisal guidance 658 recommends isatuximab plus pomalidomide and dexamethasone for use within the Cancer Drugs Fund as a treatment option for adults who have had 3 previous therapies including lenalidomide and a proteasome inhibitor, and whose disease has progressed on their last treatment. This recommendation is the subject of this evaluation.

The technology

Isatuximab (Sarclisa, Sanofi) in combination with pomalidomide and dexamethasone has a marketing authorisation for the treatment of adult patients with relapsed and refractory multiple myeloma:

- who have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor and;

- have demonstrated disease progression on the last therapy.

Isatuximab, in combination with carfilzomib and dexamethasone, has a related marketing authorisation in the UK for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

Intervention(s)	Isatuximab in combination with pomalidomide and dexamethasone
Population(s)	Adults with relapsed or refractory multiple myeloma who have received at least 2 or more previous treatments, including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on the last therapy
Comparators	For people who have had 2 previous therapies: • ixazomib plus lenalidomide and dexamethasone (subject to NICE evaluation) For people who have had 3 previous therapies: • daratumumab

	• ixazomib plus lenalidomide and dexamethasone (subject to NICE evaluation) For people who have had 3 or more previous therapies; • pomalidomide plus dexamethasone • elranatamab (subject to NICE evaluation) • ciltacabtagene autoleucel (subject to NICE evaluation) For people who have had 4 previous therapies: • belantamab mafodotin (subject to NICE evaluation)
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rates • duration of response • time to progression • time to next treatment • time to treatment discontinuation • 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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should 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	**Related Technology Appraisals:** Carfilzomib with daratumumab and dexamethasone for treating relapsed or refractory multiple myeloma. NICE technology appraisal guidance 841. Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (2022) NICE technology appraisal guidance 783. Review date 2025. Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma (2020) NICE technology appraisal guidance 658. Review in progress. Lenalidomide for the treatment of multiple myeloma in people who have received at least 2 prior therapies (2019) NICE Technology appraisal guidance 171. Review date not stated. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (2018) NICE technology appraisal guidance 505. Review in progress. Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (2017) NICE Technology appraisal guidance 427. Review date not stated. Panobinostat for treating multiple myeloma after at least 2 previous treatments (2016) NICE Technology appraisal guidance 380. Review date not stated. **Related appraisals in development:** Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (CDF review of TA505) NICE technology appraisal guidance [ID1635]. Publication expected February 2023. Belantamab mafodotin for treating relapsed or refractory multiple myeloma after 4 or more therapies. NICE technology appraisal guidance [ID2701]. Publication expected June 2023. Elranatamab for treating refractory multiple myeloma after 3 standard therapies. NICE technology appraisal guidance [ID4026]. Publication expected February 2024. Teclistamab for treating relapsed or refractory multiple myeloma after 3 therapies NICE technology appraisal guidance [ID5087]. Publication date to be confirmed. Ciltacabtagene autoleucel for treating relapsed and lenalidomide-refractory multiple myeloma after 1 to 3 therapies NICE technology appraisal guidance [ID4012]. Publication date to be confirmed. Idecabtagene vicleucel for treating relapsed and refractory multiple myeloma in people who have received at least 3 prior

	therapies. NICE technology appraisal guidance [ID1442]. Publication date to be confirmed. Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma NICE technology appraisal guidance [ID3797]. Publication date to be confirmed. Talquetamab for treating relapsed or refractory multiple myeloma after 3 therapies NICE technology appraisal guidance [ID5082]. Publication date to be confirmed. **Related Guidelines:** Myeloma: diagnosis and management (2018) NICE guideline 35. Review date not stated. 'Haematological cancers: improving outcomes' (2016). NICE guidance 47. No current plans to review this guidance. **Related Quality Standards** Haematological cancers (2017) NICE quality standard 150.
Related National Policy	NHS England (2020) Bendamustine for relapsed multiple myeloma (all ages). Clinical Commissioning Policy. Reference: 200604P The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019)

References

1. Cancer Research UK . Myeloma incidence statistics. Accessed 8 December 2022.

2. United Kingdom Fact sheet, International Agency for Research on Cancer. Accessed 8 December 2022.

3. Cancer Research UK. Myeloma survival statistics. Accessed 8 December 2022.

4. Cancer Research UK. Myeloma statistics. Accessed 8 December 2022.