

## Appendix B

### NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

#### Health Technology Evaluation

#### Isatuximab in combination for untreated multiple myeloma when a stem cell transplant is unsuitable ID3981

#### Final scope

##### Remit/evaluation objective

To appraise the clinical and cost effectiveness of isatuximab in combination within its marketing authorisation for treating multiple myeloma when a stem cell transplant is unsuitable.

##### 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 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 (as a result of anaemia), infections, hypercalcaemia (too much calcium in the blood) and kidney problems.<sup>1</sup>

There were around 5,000 newly diagnosed cases of multiple myeloma in England in 2021, mostly in people aged 65 years and over.<sup>2</sup> Multiple myeloma is more common in men than in women and incidence rates are reported to be higher in people of African ethnic group.<sup>3</sup> The 5-year survival rate for adults with multiple myeloma in England and Wales is about 56%.<sup>4</sup>

Multiple myeloma is an incurable disease, and treatment aims 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 917](#) recommends daratumumab with lenalidomide and dexamethasone as an option for untreated multiple myeloma in adults when an autologous stem cell transplant is unsuitable, and [NICE technology appraisal 587](#) recommends lenalidomide plus dexamethasone in adults who are not eligible for a stem cell transplant, if thalidomide is contraindicated (including for pre-existing conditions that it may aggravate) or the person cannot tolerate thalidomide.

[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, or bortezomib in combination with an alkylating agent and a corticosteroid if thalidomide is contraindicated or the person cannot tolerate thalidomide. However, thalidomide-based combinations are no longer regularly used in NHS practice, as outlined by clinical experts in [NICE technology appraisal 917](#).

Final scope for the evaluation of isatuximab in combination for untreated multiple myeloma when a stem cell transplant is unsuitable ID3981

## Appendix B

### The technology

Isatuximab (Sarclisa, Sanofi) does not currently have a marketing authorisation in the UK for treating untreated multiple myeloma when a stem cell transplant is unsuitable. It has been studied in a clinical trial in people with newly diagnosed multiple myeloma who are ineligible for transplant. The trial compared isatuximab in combination with bortezomib, lenalidomide and dexamethasone with treatment with bortezomib, lenalidomide and dexamethasone (also known as VRd).

<b>Intervention(s)</b>	Isatuximab with bortezomib, lenalidomide and dexamethasone
<b>Population(s)</b>	Adults with untreated multiple myeloma when stem cell transplant is unsuitable
<b>Comparators</b>	<ul style="list-style-type: none"><li>• Daratumumab with lenalidomide and dexamethasone</li><li>• Lenalidomide with dexamethasone</li><li>• Bortezomib with alkylating agent and corticosteroid (such as cyclophosphamide and dexamethasone)</li></ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"><li>• overall survival</li><li>• progression-free survival</li><li>• response rates</li><li>• time to treatment discontinuation</li><li>• minimal residual disease-negative status</li><li>• adverse effects of treatment</li><li>• health-related quality of life.</li></ul>
<b>Economic analysis</b>	<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.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p>

Final scope for the evaluation of isatuximab in combination for untreated multiple myeloma when a stem cell transplant is unsuitable ID3981

## Appendix B

<b>Other considerations</b>	<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>
<b>Related NICE recommendations</b>	<p><b>Related technology appraisals:</b></p> <p><a href="#">Daratumumab with lenalidomide and dexamethasone for untreated multiple myeloma when a stem cell transplant is unsuitable</a> (2023) NICE technology appraisal guidance 917.</p> <p><a href="#">Daratumumab in combination for untreated multiple myeloma when a stem cell transplant is suitable</a> (2022) NICE technology appraisal guidance 763.</p> <p><a href="#">Lenalidomide plus dexamethasone for previously untreated multiple myeloma</a> (2019) NICE technology appraisal guidance 587.</p> <p><a href="#">Bortezomib and thalidomide for the first-line treatment of multiple myeloma</a> (2015) NICE technology appraisal guidance 228.</p> <p><b>Related Guidelines:</b></p> <p><a href="#">‘Myeloma: diagnosis and management’</a> (2018). NICE guideline 35.</p> <p><a href="#">‘Haematological cancers: improving outcomes’</a> (2016). NICE guidance 47.</p> <p><b>Related Quality Standards:</b></p> <p><a href="#">‘Haematological cancers’</a> (2017) NICE quality standard 150.</p>
<b>Related National Policy</b>	<p>The NHS Long Term Plan (2019) <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2023) <a href="#">Manual for prescribed specialist services (2023/2024)</a></p>

### References

1. Cancer Research UK (2023) [Myeloma](#). Accessed July 2024
2. NHS Digital (2023) [Cancer registration statistics, 2021](#). Accessed July 2024
3. Cancer Research UK (2023) [Myeloma incidence](#). Accessed July 2024
4. NHS Digital (2023) [Cancer Survival in England, cancers diagnosed 2016 to 2020, followed up to 2021](#). Accessed July 2024

Final scope for the evaluation of isatuximab in combination for untreated multiple myeloma when a stem cell transplant is unsuitable ID3981