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

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of isatuxmab 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.[1]

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

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.

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).

Intervention(s)	Isatuximab with bortezomib, lenalidomide and dexamethasone
Population(s)	Adults with untreated multiple myeloma when stem cell transplant is unsuitable
Comparators	• Bortezomib with alkylating agent and corticosteroid • Daratumumab with lenalidomide and dexamethasone For people who are unable to tolerate, or have contraindications to thalidomide: • Lenalidomide with dexamethasone • Thalidomide with alkylating agent and corticosteroid
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • minimal residual disease-negative status • 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:** Daratumumab with lenalidomide and dexamethasone for untreated multiple myeloma when a stem cell transplant is unsuitable (2023) NICE technology appraisal guidance 917. Daratumumab in combination for untreated multiple myeloma when a stem cell transplant is suitable (2022) NICE technology appraisal guidance 763. Lenalidomide plus dexamethasone for previously untreated multiple myeloma (2019) NICE technology appraisal guidance 587. Bortezomib and thalidomide for the first-line treatment of multiple myeloma (2015) NICE technology appraisal guidance 228. **Related Guidelines:** 'Myeloma: diagnosis and management' (2018). NICE guideline 35. 'Haematological cancers: improving outcomes' (2016). NICE guidance 47. **Related Quality Standards:** 'Haematological cancers' (2017) NICE quality standard 150.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024)

Questions for consultation

Are thalidomide combination treatments still commonly used in NHS practice in England for multiple myeloma when stem cell transplant is unsuitable? Would bortezomib with an alkylating agent and corticosteroid or lenalidomide with dexamethasone ever be used as a first line treatment where thalidomide combination treatments could be tolerated or was not contraindicated?

Have all the relevant comparators been included in the scope?

Where do you consider isatuximab will fit into the existing care pathway for multiple myeloma?

Would isatuximab be a candidate for managed access?

Do you consider that the use of isatuximab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which isatuximab will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Cancer Research UK (2023) Myeloma. Accessed March 2024

2. NHS Digital (2023) Cancer registration statistics, 2021. Accessed March 2024

3. Cancer Research UK (2023) Myeloma incidence. Accessed March 2024

4. NHS Digital (2023) Cancer Survival in England, cancers diagnosed 2016 to 2020, followed up to 2021. Accessed March 2024