NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Idecabtagene vicleucel for treating relapsed and refractory multiple myeloma in people who have received at least 3 prior therapies

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of idecabtagene vicleucel within its marketing authorisation for treating relapsed and refractory multiple myeloma in people who have received at least 3 prior therapies.

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 2017, 5,034 people were diagnosed with multiple myeloma in England.[1] It is most frequently diagnosed in older people, with 43% of new cases in England in people aged 75 years and over.[2] 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.[3] The 5-year survival rate for adults with multiple myeloma in England is about 52%.[4]

Multiple myeloma is an incurable disease. Therapy aims to prolong survival and maintain a good quality of life by controlling the disease and relieving symptoms. Some people may be eligible for stem-cell transplants. NICE guidance recommends thalidomide or bortezomib in combination with an alkylating agent and corticosteroid (NICE technology appraisal guidance 228) or lenalidomide in combination with dexamethasone (NICE technology appraisal guidance 587) as options for untreated multiple myeloma. If the disease progresses after initial treatment, the choice of subsequent therapy is influenced by previous treatment and response to it, the duration of remission, comorbidities and patient preference.

For people whose disease is relapsed or refractory after at least 1 prior therapy:

- NICE technology appraisal guidance 129 recommends bortezomib monotherapy as a treatment option for people who have received 1 previous therapy.

- NICE technology appraisal guidance 457 recommends carfilzomib in combination with dexamethasone as a treatment option for people who have received only 1 previous therapy, which did not include bortezomib.

- NICE technology appraisal guidance 573 recommends daratumumab in combination with bortezomib and dexamethasone for use within the Cancer Drugs Fund after 1 previous therapy.

- NICE technology appraisals guidance 586 recommends lenalidomide in combination with dexamethasone as a treatment option for people who have received 1 previous therapy

For people who have had at least 2 prior therapies:

- NICE technology appraisal guidance 171 recommends lenalidomide in combination with dexamethasone as a treatment option for people who have received 2 or more previous therapies.

- NICE technology appraisal guidance 380 recommends panobinostat in combination with bortezomib and dexamethasone as a treatment option for people who have received at least 2 previous therapies including bortezomib and an immunomodulatory agent.

- NICE technology appraisal guidance 505 recommends ixazomib citrate in combination with lenalidomide and dexamethasone for use within the Cancer Drugs Fund after 2 or 3 previous therapies.

For people who have had at least 3 prior therapies:

- NICE technology appraisal guidance 427 recommends pomalidomide in combination with low-dose dexamethasone as a treatment option after 3 previous therapies including both lenalidomide and bortezomib.

- NICE technology appraisal guidance 510 recommends daratumumab monotherapy for use within the Cancer Drugs Fund after 3 previous therapies.

The technology

Idecabtagene vicleucel (brand name unknown, Celgene, a BMS company) is a chimeric antigen receptor (CAR) T-cell therapy that changes a patient's T cells to target a protein called BCMA, which is highly expressed on myeloma cells. Idecabtagene vicleucel is administered as a single intravenous infusion.

Idecabtagene vicleucel does not currently have a marketing authorisation in the UK for multiple myeloma. It is being studied in a single arm clinical trial for relapsed and refractory multiple myeloma in adults who have received at least 3 previous treatments including a proteasome inhibitor (such as bortezomib, carfilzomib or ixazomib citrate), an immunomodulatory agent (such as lenalidomide, thalidomide or pomalidomide) and an anti-CD38 antibody (such as daratumumab).

Intervention(s)	Idecabtagene vicleucel
Population(s)	People with relapsed and refractory multiple myeloma who have had at least 3 previous treatments

Comparators	• Pomalidomide in combination with dexamethasone • Panobinostat in combination with bortezomib and dexamethasone • Conventional chemotherapy regimens (for example, melphalan and cyclophosphamide) • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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, comparator technologies and subsequent therapies (such as treatment for cytokine release syndrome) will 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 and NICE Pathways	**Related Technology Appraisals:** Daratumumab monotherapy for treating relapsed and refractory multiple myeloma (2018) NICE technology appraisals guidance 510. Review date November 2020. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (2018) NICE technology appraisals guidance 505. Review date December 2019.

	Pomalidomide for multiple myeloma previously treated with lenalidomide and bortezomib (2017) NICE technology appraisals guidance 427. Review date 2020. **Terminated appraisals:** Pomalidomide with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma (2019) NICE technology appraisal guidance 602. (Terminated appraisal). Elotuzumab for treating relapsed or refractory multiple myeloma (2017) NICE technology appraisal guidance 434. (Terminated appraisal). Bortezomib for treating multiple myeloma after second or subsequent relapse (2017) NICE technology appraisal guidance 453. (Terminated appraisal) Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (2017) NICE technology appraisal guidance 454 (Terminated appraisal). **Appraisals in development (including suspended appraisals):** Selinexor with low-dose dexamethasone for treating refractory multiple myeloma. NICE technology appraisals guidance [ID1535]. Publication expected January 2021. Isatuximab with carfilzomib and dexamethasone for treating relapsed or refractory multiple myeloma. NICE technology appraisals guidance [ID1620]. Publication date to be confirmed. Isatuximab with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma. NICE technology appraisals guidance [ID1477]. Publication expected October 2020. Belantamab mafodotin for treating relapsed or refractory multiple myeloma after 3 therapies. NICE technology appraisal guidance [ID2701]. Publication date to be confirmed. Carfilzomib with daratumumab and dexamethasone for treating relapsed or refractory multiple myeloma. NICE technology appraisal guidance [ID2709]. Publication date to be confirmed. Pembrolizumab for previously treated multiple myeloma. NICE technology appraisals guidance [ID1139]. Suspended August 2017. Plitidepsin in combination with dexamethasone for treating relapsed or refractory multiple myeloma. NICE technology appraisals guidance [ID1081]. Suspended April 2018. **Related Guidelines:** Haematological cancers: improving outcomes (2016) NICE

	guideline 47 Myeloma: diagnosis and management (2016) NICE guideline 35. Last updated October 2018. **Related Quality Standards:** Haematological cancers (2017) NICE quality standard 150 **Related NICE Pathways:** Myeloma (2018) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Blood and marrow transplantation services (adults and children) [section 29, page 98], specialist cancer services (adults) [section 105, page 274]. Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 4, 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for idecabtagene vicleucel been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for relapsed and refractory multiple myeloma in people who have had at least 3 previous treatments?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom idecabtagene vicleucel is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider idecabtagene vicleucel will fit into the existing NICE pathway, 'Myeloma'?

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 idecabtagene vicleucel 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.

Do you consider idecabtagene vicleucel to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of idecabtagene vicleucel can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

[1] Cancer Research UK. Available from: 'Myeloma incidence by sex and UK region'. Accessed June 2020.

[2] Office of national statistics. Available from: 'Cancer registration statistics, England'. Accessed June 2019.

[3] National cancer institute. Available from: 'SEER Cancer Statistics Review, 1975-2008'. Accessed June 2019.

[4] Cancer Research UK Available from: 'Myeloma survival'. Accessed June 2020.