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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Ciltacabtagene autoleucel for treating relapsed or refractory multiple myeloma

Final scope

Final remit/appraisal objective

To appraise the clinical and cost effectiveness of ciltacabtagene autoleucel within its marketing authorisation for relapsed or 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 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.

There were 5,034 newly diagnosed cases of multiple myeloma in England in 2017.[1] Of these 43% where in people aged 75 years and over.[1] 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. The 5-year survival rate for adults with multiple myeloma in England and Wales is about 50%.[2]

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. 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 3 or more prior therapies:

- NICE technology appraisal guidance 171 recommends lenalidomide plus dexamethasone as a treatment option for people who have had at least 2 previous 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 380 recommends panobinostat plus bortezomib and dexamethasone as a treatment option for adults who have had at least 2 previous 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.

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- NICE technology appraisal guidance 510 recommends daratumumab monotherapy for use within the Cancer Drugs Fund as a treatment option for adults who have had 3 previous therapies including a proteasome inhibitor and an immunomodulator.

- NICE technology appraisal guidance 658 recommends isatuximab with 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.

The technology

Ciltacabtagene autoleucel (brand name unknown, Janssen) is a chimeric antigen receptor T-cell (CAR-T) therapy that targets the B cell maturation antigen (BCMA) protein which is expressed only on plasma cells. Binding of ciltacabtagene autoleucel to BCMA prevents B-cell maturation and differentiation into plasma cells. Ciltacabtagene autoleucel is administered as a single intravenous infusion.

Ciltacabtagene autoleucel does not have a marketing authorisation in the UK for relapsed or refractory multiple myeloma. It is being studied in a single arm trial in adults with relapsed or refractory multiple myeloma who have had at least 3 previous therapies.

Intervention(s)	Ciltacabtagene autoleucel
Population(s)	Adults with relapsed/refractory multiple myeloma who have had at least 3 previous therapies
Comparators	For people who have had 3 previous therapies, depending on previous therapy: • panobinostat plus bortezomib and dexamethasone • pomalidomide plus dexamethasone
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rates (for example complete response) • time to next treatment • adverse effects of treatment • health-related quality of life.

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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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technologies appraisal guidance for the same indication a cost comparison may be carried out. 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.
Other considerations	If the evidence allows, subgroup analyses based on type and number of lines of previous therapy will be considered. 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:** Isatuximab with pomalidomide and dexamethasone for treating relapsed and refractory multiple myeloma. (2020) NICE technology appraisal guidance 658. Review date expected 2023. Carfilzomib for previously treated multiple myeloma. (2020) NICE technology appraisal guidance 657. Review date 2023. Lenalidomide plus dexamethasone for multiple myeloma after 1 treatment with bortezomib. (2019) NICE technology appraisal guidance 586. Review date expected 2022. Daratumumab with bortezomib and dexamethasone for previously treated multiple myeloma. (2019) NICE technology appraisal guidance 573. Review date expected 2021. Daratumumab monotherapy for treating relapsed and refractory multiple myeloma. (2018) NICE technology appraisal guidance 510. Review date expected 2021. Ixazomib with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma. (2018) NICE technology appraisal guidance 505. Review date expected 2021. Pomalidomide for multiple myeloma previously treated with

	lenalidomide and bortezomib (2017) NICE technology appraisal guidance 427. Review date expected 2021 Panobinostat for treating multiple myeloma after at least 2 previous treatments. (2016) NICE technology appraisal guidance 380. Guidance on static list 2019. Lenalidomide for the treatment of multiple myeloma in people who have received at least 2 prior therapies. (2009). NICE technology appraisal guidance 171. Guidance on static list 2014. Bortezomib monotherapy for relapsed multiple myeloma. (2007) NICE technology appraisal guidance 129. Guidance on static list 2012. **Terminated appraisals:** Pomalidomide with bortezomib and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2019) NICE technology appraisal guidance 602. Bortezomib for treating multiple myeloma after second or subsequent relapse (terminated appraisal) (2017) NICE technology appraisal guidance 453. Daratumumab with lenalidomide and dexamethasone for treating relapsed or refractory multiple myeloma (terminated appraisal) (2017) NICE technology appraisal guidance 454. Elotuzumab for previously treated multiple myeloma (terminated appraisal) (2017) NICE technology appraisal guidance 434. **Appraisals in development (including suspended appraisals):** Carfilzomib with dexamethasone and lenalidomide for treating multiple myeloma after at least 1 previous therapy (update of TA457) [ID1493]. Publication expected 2021. Carfilzomib with daratumumab and dexamethasone for treating relapsed or refractory multiple myeloma [ID2709]. Publication expected 2022. Selinexor with bortezomib and low-dose dexamethasone for treating relapsed refractory multiple myeloma [ID3797]. Publication expected 2022. Idecabtagene vicleucel for treating relapsed and refractory multiple myeloma in people who have received at least 3 prior therapies publication expected [ID1442]. Publication date to be confirmed. Elotuzumab for multiple myeloma [ID966]. [Suspended]. Elotuzumab with pomalidomide and dexamethasone for treating multiple myeloma after 2 therapies [ID1467]. [Suspended]. Daratumumab with pomalidomide and dexamethasone for treating relapsed or refractory multiple myeloma [ID3775].

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	[Suspended] Isatuximab with carfilzomib and dexamethasone for treating relapsed or refractory multiple myeloma [ID1620]. [Suspended] Ixazomib with lenalidomide and dexamethasone for untreated multiple myeloma [ID1170] [Suspended]. Pembrolizumab for previously treated multiple myeloma [ID1139]. [Suspended]. Pelareorep for treating relapsed or refractory multiple myeloma [ID1028] [Suspended] Plitidepsin in combination with dexamethasone for treating relapsed or refractory multiple myeloma [ID1081]. [Suspended]. Selinexor with low-dose dexamethasone for treating refractory multiple myeloma [ID1535]. [Suspended]. Vorinostat in combination with bortezomib for the treatment of multiple myeloma in people who have received at least one prior therapy [ID501]. [Suspended]. **Related Guidelines:** Haematological cancers: improving outcomes (2016) NICE guideline 47 Myeloma: diagnosis and management (2016) NICE guideline 35 **Related Quality Standards:** Haematological cancers (2017) NICE quality standard 150 **Related NICE Pathways:** Myeloma (2017) 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, pages 98-100] Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1 Office of national statistics 'Cancer registration statistics, England'. (2017) Accessed November 2020.

2 Cancer Research UK 'Myeloma'. Accessed November 2020.

