Report CARVYKTI®ciltacabtagene autoleucel

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance:ciltacabtagen eautoleucel **Brand Name:**Carvykti **Originator/license:**Janss en-Cilag International NV **Classification:** NCE **ATC code:** NA **Orphan Status:** **Eu:** Yes **Us:** - **Mechanism of action:**cilta-cel is a genetically modified autologous T cell immunotherapy consisting of modified T-cells bearing a CAR targeting BCMA. BCMA is primarily expressed on the surface of malignant multiple myeloma B-lineage cells, as well as late-stage B cells and plasma cells. Upon binding to BCMA-expressing cells, the CAR promotes T cell activation, expansion, and elimination of target cells[1].	**Authorized Indication:** **EMA:** cilta-celis indicated for the treatment of adult pts with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody, and have demonstrated disease progression on the last therapy[1]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:**24/03/2022 **FDA M.A. date:** - **EU Speed Approval Pathway:**No **FDA Speed Approval Pathway:**----- **ABBREVIATIONS:** **AEs:** Adverse events **BCMA:** B-cell maturation antigen **CAR:** chimeric antigen receptor **CHMP**: Committee for Medicinal Product for Human Use **CI**: Confidence Interval **Cilta-cel**: ciltacabtageneautoleucel **CR**: Complete response **ECOG**: Eastern Cooperative Oncology Group **ICANS**: immune effector cell-associated neurotoxicity syndrome **IMWG**: International Myeloma Working Group **MA**: Marketing Authorization **ORR**: overall response rate **PI**: Proteasome Inhibitor **PO**: Positive Opinion **PR**. Partial Response **Pts**: patients **SAEs**: Serious Adverse Events **Vs**.: versus	**Summary of clinical EFFICACY:** **CARTITUDE-1 (NCT03548207)**: single arm, open label, phase Ib/II study aimed to assess the safety and clinical activity of cilta-cel in adult pts (≥ 18) with relapsed or refractory multiple myeloma with poor prognosis. The study comprised a phase Ib (n=29) and a phase II (n=68), which occurred sequentially. Enrolled pts had a diagnosis of multiple myeloma per IMWG diagnostic criteria, measurable disease at screening, and an ECOG performance status score of 0 or 1. Pts must have received three or more previous lines of therapy or were double-refractory to a PI and an immunomodulatory drug, and had received a PI, immunomodulatory drug and anti-CD38 antibody. A single cilta-cel infusion (target dose $0.75x10^6$ CAR-positive viable T cells per kg) was administered5-7 days after start of lymphodepletion. The primary endpoint of phase Ib was safety and confirmation of the recommended phase II dose. The primary endpoint of phase II was ORR, defined as the proportion of pts who achieved a PR or better according to the IMWG criteria. At a median follow-up of 12.4 months, ORR was 97% (95% CI, 91.2 to 99.4), with 65 (67%) pts achieving stringent CR [2]. **Summary of clinical SAFETY:** All 97 pts had AEs. Haematological events were the most common; grade 3-4 haematological AEs were neutropenia (95%), anaemia (68%), leukopenia (61%), lymphopenia (50%). Infections occurred in 58% of pts, and the most common (≥ 10% of pts) was upper respiratory tract infection. The most common grade 3-4 infections were pneumonia (8%) and sepsis (4%). Cytokine release syndrome occurred in 95% of pts and most of them had grade 1-2. Neurotoxicity events occurred in 21% of pts and ICANS in 17%. 14 people died during the study, six of which were due to AEs considered related to the treatment (sepsis or septic shock [n=2], and cytokine release syndrome and haemophagocyticlymphohistiocytosis [n=1], lung abcess [n=1], respiratory failure [n=1], neurotoxicity [n=1])[2]. **Ongoing studies:** ● ***For the same indication:***Yes ● ***For other indications:***No **Discontinued studies (for the same indication):**No **References:** 1. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/carvykti 2. https://www.clinicalkey.com/service/content/pdf/watermarked/1-s2.0-S0140673621009338.pdf?locale=it_IT&searchIndex= 3. https://www.cancer.gov/news-events/cancer-currents-blog/2022/fda-carvykti-multiple-myeloma#:~:text=Cilta%2Dcel%20has%20a%20list,depend%20on%20their%20insurance%20coverage. 4. https://www.osservatoriomalattierare.it/i-tumori-rari/mieloma-multiplo/11572-mieloma-multiplo-30-000-i-pazienti-in-italia-incidenza-maggiore-negli-over-65#:~:text=Il%20mieloma%20multiplo%20%C3%A8%20un,5.600%20nuovi%20casi%20ogni%20anno. 5. Pick M, Vainstein V, Goldschmidt N, et al. Daratumumab resistance is frequent in advanced-stage multiple myeloma patients irrespective of CD38 expression and is related to dismal prognosis. Eur J Haematol 2018;100: 494-501 6. Usmani S, Ahmadi T, Ng Y, et al. Analysis of real-world data on overall survival in multiple myeloma patients with≥3 prior lines of therapy including a proteasome inhibitor (PI) and an immunomodulatory drug (IMiD), or double refractory to a PI and an IMiD. Oncologist 2016; 21: 1355-61. 7. M.A. Dimopoulos, P. Moreau, E. Terpos et al. Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†, Annals of Oncology, Volume 32, Issue 3, 2021, Pages 309-322	**Cost of therapy:** Cilta-cel has a list price of $465,000 for a one-time infusion [3]. **Epidemiology:** In Italy, the incidence of multiple myeloma is estimated to be 8.75 new cases per 100,000 inhabitants per year. This means around 5,600 new cases every year. It is estimated that about 30,000 pts are currently monitored or under treatment [4]. **POSSIBLE PLACE IN THERAPY** Currently, pts with triple-classrefractory multiple myeloma have notreatment options with proven clinical benefit [5-6]. Belantamabmafodotinmonotherapy or selinexor dexamethasone may be suitable options [7]. **OTHER INDICATIONS IN DEVELOPMENT:**No [7]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:**Yes (NCT04133636)[7]. **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** PHE885, Dabrafenib + Trametinib[7]. *Service reorganization Y/N: Yes *Possible off label use Y/N: No

Issued on: April 2022