Product: TECARTUS

Proper Name: Brexucabtagene autoleucel

Manufacturer: Kite Pharma, Inc.

Indication: For the treatment of adult patients with relapsed/refractory mantle cell lymphoma (r/r MCL).

Description: TECARTUS is a CD19-directed genetically modified autologous T cell immunotherapy. To prepare TECARTUS, a patient's own T cells are harvested and genetically modified ex vivo by retroviral transduction to express a chimeric antigen receptor (CAR) comprising a murine anti-CD19 single-chain variable fragment (scFv) linked to CD28 and CD3-zeta co-stimulatory domains. The anti-CD19 CAR T cells are expanded and infused back into the patient, where they can recognize and eliminate CD19-expressing target cells.

BLA: BL 125703

FDA Regulatory Milestone:

DATE	MILESTONE
6 May 2015	ZUMA-2 originally submitted, as an amendment to KTE-C19 Investigational New Drug (IND) 16278.
28 April 2016	Orphan drug designation (ODD) granted to KTE-C19 for the treatment of MCL.
16 September 2016	ZUMA-2 was re-filed under IND 16675.
15 June 2018	Breakthrough therapy designation (BTD) granted to KTE-X19 for the treatment of adults with r/r MCL.
25 September 2018	Initial multidisciplinary meeting held
23 April 2019	FDA's pre-BLA format and content written responses sent.

24 September 2019	Pre-BLA risk evaluation and mitigation strategy (REMS) meeting held.
15 November 2019	Pre-BLA topline data meeting held. Agreement reached that the provided clinical data seemed acceptable to support a BLA submission.
11 December 2019	BLA submitted.

Clinical studies to investigate brexucabtagene autoleucel in B cell malignancies were performed under BB-IND-16675, submitted in October 2015. Orphan designation for MCL was granted in April 2016, and breakthrough designation for MCL was granted in June 2018. BLA format and content were discussed in a Type B meeting in April 2019, and a preBLA Type B meeting was held in November 2019. BLA 125703 was submitted 11th December 2019, with a PDUFA action due date of 11th August 2020.

PDUFA Goal Date: August 11, 2020

FDA approval date: July 24, 2020

EMA approval date: December 14, 2020

Health Canada approval:

Japanese Ministry of Health, Labor and Welfare (MHLW) approval:

TGA approval date:

Package Insert: TECARTUS

Summary Basis for Regulatory Approval: July 23, 2020 Summary Basis for Regulatory Action - TECARTUS

European Public Assessment Report: Tecartus : EPAR - Public assessment report

Manufacturing Platform:

PARAMETER	DATA	REFERENCE
Manufacturer	Kite Pharma, Inc.	
Transgene	CD19-directed gene	1
Indication	TECARTUS is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL). This indication is approved under **accelerated approval** based on overall response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.	1
Virus & Serotype	Murine stem cell virus (MSCV)-based vector	2
Cell Substrate	Anti-CD19 chimeric antigen receptor (CAR) T cells	3
Manufacturing platform	• **PG13-CD19-H3 retroviral vector:** The PG13-CD19-H3 vector is produced constitutively from a stably-transduced PG13 (ATCC CRL-10686) cell line. For the GMP-compliant production of the retroviral vector, cells from a single vial of WCB are expanded and the culture supernatant is harvested, filtered, and filled into cryostorage bags. • **KTE-X19**: The manufacturing process of KTE-X19 starts with apheresis collection from a patient. The next steps in the manufacturing process include T-cell enrichment, T-cell activation, retroviral transduction, and T-cell expansion.	3
Dose in vial/final container	2 × 106 CAR-positive viable T cells per kg of body weight, with a maximum of 2 × 108 CAR-positive viable T cells in approximately 68 mL.	1
Dose / patient	2 × 106 CAR-positive viable T cells per kg body weight, with a maximum of 2 × 108 CAR-positive viable T cells.	1

1. Package insert: TECARTUS

2. EPAR full: Tecartus
3. EPAR quality: Tecartus : EPAR - Public assessment report
4. FDA SBAR: July 23, 2020 Summary Basis for Regulatory Action - TECARTUS

Advisory Committee:

TECARTUS is similar to other approved CD19-directed genetically modified autologous T cell immunotherapies, including YESCARTA, and did not raise new or unique scientific or regulatory issues; as a result, an advisory committee meeting was deemed not necessary.

Clinical Trials:

NCT	TRIAL PHASE	SUBJECTS ENROLLED	STUDY TITLE	COUNTRIES
Primary study				
NCT02601313	2	105	Study to evaluate the efficacy of Brexucabtagene Autoleucel (KTE-X19) in participants with relapsed/refractory Mantle Cell Lymphoma	United States, France, Germany, Netherlands
Supportive studies providing additional safety data				
NCT02614066	1, 2	125	A study evaluating Brexucabtagene Autoleucel (KTE-X19) in adult subjects with relapsed/refractory B-precursor Acute Lymphoblastic Leukemia (ZUMA-3)	United States, Canada, France, Germany, Netherlands
NCT02625480	1, 2	116	Study evaluating Brexucabtagene Autoleucel (KTE-X19) in pediatric and adolescent participants with relapsed/refractory B-precursor Acute Lymphoblastic Leukemia or relapsed/refractory B-Cell Non-Hodgkin Lymphoma	United States, Canada, France, Netherlands

NCT03624036	1	27	Safety and tolerability of Brexucabtagene Autoleucel (KTE-X19) in adults with relapsed/refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma	United States, Italy

EudraCT Numbers: None

Publications:

- Han, D., Xu, Z., Zhuang, Y., Ye, Z., & Qian, Q. (2021). Current Progress in CAR-T Cell Therapy for Hematological Malignancies. Journal of Cancer, 12(2), 326–334. https://doi.org/10.7150/jca.48976
- Maus, M. V., Alexander, S., Bishop, M. R., Brudno, J. N., Callahan, C., Davila, M. L., Diamonte, C., Dietrich, J., Fitzgerald, J. C., Frigault, M. J., Fry, T. J., Holter-Chakrabarty, J. L., Komanduri, K. V., Lee, D. W., Locke, F. L., Maude, S. L., McCarthy, P. L., Mead, E., Neelapu, S. S., Neilan, T. G., … Grupp, S. A. (2020). Society for Immunotherapy of Cancer (SITC) clinical practice guideline on immune effector cell-related adverse events. Journal for immunotherapy of cancer, 8(2), e001511. https://doi.org/10.1136/jitc-2020-001511