

New Drug Fact Blast

Clinical Services

Drug/Manufacturer:	Tecartus™ (brexucabtagene autoleucel) [Kite Pharma, Inc]
Dosage Formulations:	Cell suspension for infusion, comprising 2×10^6 CAR-positive viable T cells per kg of body weight, with a maximum of 2×10^8 CAR-positive viable T cells in approximately 68 mL
FDA Approval Date: FDB File Date:	FDA: July 24, 2020 FDB: August 2, 2020
Indication:	The treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL)
Mechanism of Action:	Chimeric antigen receptor (CAR) T-cell immunotherapy - a CD19-directed, genetically modified, autologous T-cell immunotherapy that binds to CD19-expressing cancer cells and normal B cells. Studies have demonstrated that, following anti-CD19 CAR T-cell engagement with CD19-expressing target cells, the CD28 and CD3-zeta costimulatory domains activate downstream signaling cascades that lead to T-cell activation, proliferation, acquisition of effector functions, and secretion of inflammatory cytokines and chemokines.
Dose/ Administration:	- Each single infusion bag contains a suspension of CAR-positive T cells in approximately 68 mL. The dose is 2×10^6 CAR-positive viable T cells per kg body weight, with a maximum of 2×10^8 CAR-positive viable T cells. - Autologous use only - verify the patient's identity prior to infusion. - Pre-treatment: Administer a lymphodepleting chemotherapy regimen of cyclophosphamide 500 mg/m² intravenously and fludarabine 30 mg/m² intravenously on each of the 5th, 4th, and 3rd days before infusion of Tecartus. - Pre-medicate with acetaminophen and diphenhydramine or another H1-antihistamine approximately 30 to 60 minutes prior to Tecartus infusion. Avoid use of prophylactic systemic corticosteroids as they may interfere with the activity of Tecartus. - Confirm the infusion time in advance and begin to thaw the frozen Tecartus so that it will be available for infusion when the patient is ready. Tecartus may be stored at room temperature for up to three hours. - Ensure tocilizumab (Actemra®) and emergency equipment are available prior to infusion and during the recovery period. - Infuse the entire contents of the Tecartus bag within 30 minutes. - Monitor patients at the certified healthcare facility daily for at least seven days following infusion for signs and symptoms of Cytokine Release Syndrome (CRS) and neurologic events. - Instruct patients to remain within proximity of the certified healthcare facility for at least four weeks following infusion.
Drug Clinical Highlights:	- CAR T-Cell therapy is a type of immunotherapy that involves engineering a patient's own T cells to recognize and attack cancer cells. - Tecartus is the first CAR T-cell therapy approved for the treatment of relapsed or refractory MCL. - Tecartus was granted accelerated approval, priority review, breakthrough therapy, and orphan drug designation; continued approval is based on verification of clinical benefit in confirmatory trials. - Safety and efficacy was evaluated in a single-arm, open-label, multicenter clinical trial (ZUMA-2; NCT02601313): - Enrolled 74 patients with relapsed or refractory MCL - Tecartus was successfully manufactured for 71 patients, administered to 68 patients, and 60 patients were followed for at least 6 months after their first objective disease response, making them efficacy-evaluable. - Previous therapy must have included anthracycline- or bendamustine-containing chemotherapy, an anti-CD20 monoclonal antibody, and Bruton's tyrosine kinase (BTK) inhibitor therapy with ibrutinib or acalabrutinib.

- Median number of therapies: 3 (range, 1-5)
- Previous BTK inhibitor therapy: 68 (100%)
- Relapsed or refractory to BTK inhibitor therapy: 68 (100%)
- Primary endpoint: Percentage of patients with an objective response (complete or partial response) on independent radiologic review

ZUMA-2 Efficacy Results	
Response Rate	Evaluable Patients (N=60)
Objective Response Rate ^a , n (%) [95% CI]	52 (87%) [75, 94]
Complete Response Rate, n (%) [95% CI]	37 (62%) [48, 74]
Partial Response Rate	15 (25%) [15, 38]
Duration of Response (DOR)	
Median in months [95% CI]	NR [8.6, NE]
Range ^b in months	0.0+, 29.2+
DOR, if best response is CR, median in months [95% CI]	NR [13.6, NE]
Range ^b in months	1.9+, 29.2+
DOR, if best response is PR, median in months [95% CI]	2.2 [1.5, 5.1]
Range ^b in months	0.0+, 22.1+
Median Follow-up for DOR in months ^c	8.6

CR, complete remission; NE, not estimable; NR, not reached; PR, partial remission.

a. Among all responders. DOR is measured from the date of first objective response to the date of progression or death.

b. A + sign indicates a censored value.

c. At the time of primary analysis.

- Boxed warnings:
 - Cytokine Release Syndrome (CRS):
 - CRS occurred in 91% of patients, including ≥ grade 3 CRS in 18% of patients.
 - Do not administer to patients with active infections or inflammatory disorders.
 - Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.
 - Neurologic toxicities, including life-threatening reactions, may occur concurrently with CRS or after CRS resolution:
 - Neurologic events occurred in 81% of patients, 37% of whom experienced grade 3 or higher (severe or life-threatening) adverse reactions.
 - Monitor after treatment and provide supportive care and/or corticosteroids as needed.
 - Only available through the Yescarta and Tecartus REMS Program:
 - Certified healthcare facilities must have on-site, immediate access to tocilizumab and ensure that a minimum of two doses of tocilizumab are available for each patient for infusion within two hours after Tecartus infusion, if needed for treatment of CRS.
 - Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense, or administer Tecartus are trained in the management of CRS and neurologic toxicities.
- Contraindications: none
- Warnings:
 - Hypersensitivity reactions including anaphylaxis may occur due to dimethyl sulfoxide (DMSO) or residual gentamicin in Tecartus.
 - Severe infections: infections (all grades) occurred in 56% of patients; grade 3 or higher infections occurred in 30% of patients.
 - Prolonged cytopenias: monitor blood counts after infusion.
 - Hypogammaglobulinemia: monitor immunoglobulin levels after treatment.
 - Secondary malignancies: monitor life-long after treatment.
 - Patients should refrain from driving or operating heavy equipment for at least 8 weeks after therapy.

	Adverse reactions (incidence $\geq 20\%$): pyrexia, CRS, hypotension, encephalopathy, fatigue, tachycardia, arrhythmia, infection – pathogen unspecified, chills, hypoxia, cough, tremor, musculoskeletal pain, headache, nausea, edema, motor dysfunction, constipation, diarrhea, decreased appetite, dyspnea, rash, insomnia, pleural effusion, and aphasia																								
Disease State Clinical Highlights:	- Mantle cell lymphoma (MCL) is a rare B-cell non-Hodgkin lymphoma typically occurring in men over the age of 60. - MCL usually responds well to first-line therapy however most patients develop recurring disease. In relapsed lymphoma, the disease reappears or grows again after a period of remission, while in refractory lymphoma, the disease does not respond to treatment or responds only briefly. - Approximately 7% of adult non-Hodgkin lymphomas are MCL, with an incidence estimated at 4-8 cases per million persons per year in the United States and Europe.																								
Price Per Unit (WAC):	\$373,000.00 for a one-time infusion																								
Therapeutic Alternatives:	- Tecartus is the third FDA approved CAR T-cell therapy, after Kymriah® and Yescarta®. While Tecartus shares the same design as Yescarta, also made by Kite Pharma, Inc., the difference lies in the manufacturing process. Tecartus undergoes a white blood cell enrichment process, which is necessary for certain types of B-cell blood cancers, such as MCL, where circulating lymphoblasts are a common feature. <table><tr><th>CAR T-Cell Therapies</th><th>Kymriah® (tisagenlecleucel)</th><th>Yescarta® (axicabtagene ciloleucel)</th><th>Tecartus™ (brexucabtagene autoleucel)</th></tr><tr><td>Indications</td><td> - Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse - Adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma </td><td> - Adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma </td><td> - Adult patients with relapsed or refractory mantle cell lymphoma (MCL) </td></tr><tr><td>Incidence of CRS</td><td> 79% in ALL 74% in DLBCL </td><td> 94% </td><td> 91% </td></tr><tr><td>Incidence of Neurological Toxicities</td><td> 72% in ALL 58% in DLBCL </td><td> 87% </td><td> 81% </td></tr><tr><td>Cost per infusion</td><td>\$373,000.00 WAC</td><td>\$373,000.00 WAC</td><td>\$373,000.00 WAC</td></tr><tr><td>Manufacturer</td><td>Novartis</td><td>Kite Pharma, Inc.</td><td>Kite Pharma, Inc.</td></tr></table> - Treatment options for the management of relapsed/refractory MCL: - FDA approved agents – any of these may be used with rituximab: - Bortezomib (Velcade®) - Lenalidomide (Revlimid®) - BTK inhibitors: - Ibrutinib (Imbruvica®) - Acalabrutinib (Calquence®) - Zanubrotinib (Brukinsa™) - Other common therapies: - Bendamustine, with or without rituximab - Combination chemotherapy, with or without rituximab - Stem cell transplant	CAR T-Cell Therapies	Kymriah® (tisagenlecleucel)	Yescarta® (axicabtagene ciloleucel)	Tecartus™ (brexucabtagene autoleucel)	Indications	- Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse - Adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma	Adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma	Adult patients with relapsed or refractory mantle cell lymphoma (MCL)	Incidence of CRS	79% in ALL 74% in DLBCL	94%	91%	Incidence of Neurological Toxicities	72% in ALL 58% in DLBCL	87%	81%	Cost per infusion	\$373,000.00 WAC	\$373,000.00 WAC	\$373,000.00 WAC	Manufacturer	Novartis	Kite Pharma, Inc.	Kite Pharma, Inc.
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	NCCN Guidelines state Tecartus is recommended for the treatment of adult patients with relapsed or refractory MCL only after chemoimmunotherapy and BTK inhibitor therapy.
Prior Authorization Approval Criteria:	Must meet the following criteria: <u>Initial Therapy:</u> - Prescribed by or in consultation with an oncologist, hematologist, or other specialist in the treated disease state - Participant aged ≥ 18 years - Participant is currently not pregnant - Documented diagnosis of relapsed or refractory mantle cell lymphoma (MCL) (ICD-10 C83.1) - Documentation of two or more previous lines of systemic therapy for MCL, including chemoimmunotherapy and BTK inhibitor therapy - No previous history of CAR T-cell therapy - No active infections or inflammatory disorders <u>Continuation of Therapy:</u> - None Additional Provider Diagnostic/Monitoring Criteria, if desired: - Participant has an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 1 (patient must be healthy enough to participate in the pre-treatment lymphodepleting chemotherapy regimen and the collection and cultivation [leukapheresis] process as well as to withstand potential cytokine release syndrome, neurologic toxicities, and prolonged cytopenias). - Tecartus has not been studied in patients with creatinine clearance ≤ 60 mL/min; patients with cardiac ejection fraction $< 50\%$; patients with HIV, hepatitis B, hepatitis C, seizure disorders, cerebrovascular ischemia, dementia, cerebral edema, or any autoimmune disease with CNS involvement. - Vaccination with live virus vaccines is not recommended for at least six weeks prior to the start of lymphodepleting chemotherapy, during treatment with Tecartus, and until immune recovery following treatment.
Implication to State Medicaid Program:	- LOE: 5/30/2031 or 5/27/2036 - In ZUMA-2, two patients, who developed disease progression after achieving an objective response in the first infusion, received a second course of Tecartus approximately 1 year after the initial infusion. Analysis of these 2 patients is ongoing. Depending upon the outcomes of these 2 patients, a second course of therapy could be possible. - Tecartus is also being studied in relapsed and refractory acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), and B-cell non-Hodgkin lymphoma.

References:

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10. Understanding chimeric antigen receptor (CAR) T cell technology. Kite Pharma, Inc. <https://www.kitepharma.com/-/media/kite/images/news/mediakit/understanding-chimeric-antigen-receptor.pdf>. April 2020.

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