Clinical Criteria

Subject:	**Tecartus (brexucabtagene autoleucel)**		
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Overview

This document addresses the use of Tecartus (brexucabtagene autoleucel), a CD19-directed immunotherapy, for treatment of relapsed or refractory mantle cell lymphoma (MCL).

Tecartus is a CD19-directed, genetically-modified autologous T-cell immunotherapy, also known as chimeric antigen receptor (CAR) T-cell therapy. CAR T-cells are made by first collecting T-cells from the patient. The cells are then sent to a laboratory where they are genetically engineered to produce chimeric antigen receptors. The modified T-cells, now known as CAR T-cells, have the ability to better recognize an antigen (the CD19 protein) on targeted tumor cells. After the CAR T-cells have multiplied in the laboratory, they are then infused back into the patient. The modified CAR T-cells help the body's immune system better target and treat the tumor cells.

While Tecartus shares the same design as another FDA-approved anti-CD19 CAR-T cell therapy (axicabtagene ciloleucel), the difference lies in the manufacturing process for Tecartus. Tecartus undergoes a white blood cell enrichment process, which is necessary for certain types of B-cell blood cancers, such as mantle cell lymphoma, where circulating lymphoblasts are a common feature.

Tecartus is the first CAR-T therapy indicated for relapsed or refractory mantle cell lymphoma. In mantle cell lymphoma, cancerous B-cells are found in a region of the lymph node called the mantle zone. Mantle cell lymphomas are considered slow growing cancers, and usually widespread by the time it is diagnosed (NIH 2016).

The FDA has approved Tecartus for relapsed or refractory mantle cell lymphoma under its accelerated approval program. Continued approval is based on verification of clinical benefit in confirmatory trials.

Tecartus has a black box warning for cytokine release syndrome (CRS), and should not be administered in patients with active infection or inflammatory disorders due to risk of life-threatening reactions and death. Severe or life-threatening CRS should be treated with tocilizumab with or without corticosteroids. Tecartus also has black box warning for causing neurological toxicities, which could also be severe and life-threatening. Monitoring for neurological events after administration is recommended. Due to these black box warnings, Tecartus is only available through a Risk Evaluation and Mitigation Strategy (REMS) program.

Definitions and Measures

Allogeneic cells: Harvested from a histocompatible donor.

Autologous cells: Harvested from the individual's own cells.

Bone marrow: A spongy tissue located within flat bones, including the hip and breast bones and the skull. This tissue contains stem cells, the precursors of platelets, red blood cells, and white cells.

Chemotherapy: The medical treatment of a disease, particularly cancer, with drugs or other chemicals.

Chimerism: Cell populations derived from different individuals; may be mixed or complete.

ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:

- **0 = Fully active, able to carry on all pre-disease performance without restriction**
- **1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light house work, office work**
- **2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours**
- **3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours**
- **4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair**
- **5 = Dead**

Kinase inhibitor: Type of drug which works by blocking several enzymes that promote cell growth, which has been found to be an effective approach to treat a variety of cancers.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Tecartus (brexucabtagene autoleucel)

Requests for Tecartus (brexucabtagene autoleucel) may be approved if the following criteria are met:

I. **Individual is 18 years of age or older; AND**
II. **Individual has a diagnosis of mantle cell lymphoma (MCL); AND**
III. **Individual has at least one (1) measurable lesion; AND**
IV. **Individual has a histological confirmation of one of the following (Wang 2020):**
   A. **Cyclin D1 overexpression; OR**
   B. **Presence of the translocation t(11;14); AND**
V. **Individual has relapsed or refractory disease after *all* of the following (which may or may not include therapy supported by autologous stem cell transplant) (Wang 2020):**
   A. **Anthracycline- or bendamustine- containing chemotherapy; AND**
   B. **Anti-CD20 monoclonal antibody, such as rituximab; AND**
   C. **Bruton's tyrosine kinase (BTK) inhibitor, such as ibrutinib, acalabrutinib, or zanubrutinib; AND**
VI. **Individual has adequate bone marrow reserve defined by all of the following (Wang 2020, NCT02601313):**
   A. **Absolute neutrophil count (ANC) ≥ 1000 cells/µL; AND**
   B. **Absolute lymphocyte count (ALC) greater than or equal to 100 cells/µL; AND**
   C. **Platelet count greater than or equal to 75,000 cells/µL; AND**
VII. **Individual has a current ECOG performance status of 0-1 (Wang 2020); AND**
VIII. **Individual is using as a one-time, single administration treatment.**

Requests for Tecartus (brexucabtagene autoleucel) may not be approved for the following (Wang 2020, NCT02601313):

I. **Repeat administration; OR**
II. **Creatinine clearance (as estimated by Cockcroft Gault) less than 60 mL/min; OR**
III. **Cardiac ejection fraction (EF) less than 50%; OR**
IV. **Evidence of pericardial effusion as determined by an echocardiogram (ECHO), or other significant ECHO findings; OR**
V. **History of a seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, cerebral edema, or posterior reversible encephalopathy syndrome; OR**
VI. **Any autoimmune disease with central nervous system (CNS) involvement; OR**
VII. **Active or latent hepatitis B, active hepatitis C, human immunodeficiency virus (HIV) positive, or other active, uncontrolled infection; OR**

VIII. Using in combination with other chemotherapy agents (not including the use of lymphodepleting chemotherapy as labeled prior to Tecartus infusion); OR

IX. History of allogeneic stem cell transplant, chimeric antigen receptor therapy or other genetically modified T-cell therapy, including, but not limited to, previous administration of Tecartus, axicabtagene ciloleucel, or tisagenlecleucel; OR

X. When the above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9999	Not otherwise classified, antineoplastic drugs
J3590	Unclassified biologics
J3490	Unclassified drugs

ICD-10 Diagnosis

All diagnosis

Document History

New: 08/21/2020
Document History:

- 08/21/2020 – Annual Review: Add new clinical criteria document for Tecartus (brexucabtagene autoleucel) for mantle-cell lymphoma. Coding reviewed: Added HCPCS J9999, J3590, J3490. All diagnosis pend

References

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3. NCT02601313. ClinicalTrials.gov. U.S. National Library of Medicine. Available at https://clinicaltrials.gov/ct2/show/NCT02601313?term=nct02601313&draw=2&rank=1. Accessed on July 27, 2020.
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5. Wang M, Munoz J, Goy A, et al. Supplementary Appendix to KTE-X19 CAR T-cell therapy in relapsed or refractory mantle-cell lymphoma. N Engl J Med 2020;382:1331-42. Accessed July 27, 2020.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.