Medical Drug Clinical Criteria

Subject:	Tecartus (brexucabtagene autoleucel)		
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Overview

This document addresses the use of Tecartus (brexucabtagene autoleucel), a CD19-directed immunotherapy that is used to treat relapsed or refractory mantle cell lymphoma (MCL) and B-cell precursor acute lymphoblastic leukemia (ALL).

The FDA approved indications for Tecartus include adults with B-cell precursor acute lymphoblastic leukemia (also called acute lymphocytic leukemia) that is relapsed or refractory, and for adults 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 from follicular lymphoma.

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 a 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.

The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the following uses:

- Acute Lymphoblastic Leukemia
- Mantle Cell Lymphoma

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) for **B-cell acute lymphoblastic leukemia (ALL)** may be approved if the following criteria are met (Label, NCCN 2A, NCT02614066):

I. Individual is 18 years of age or older; **AND**
II. Individual has diagnosis of B-cell acute lymphoblastic leukemia; **AND**
III. Individual has confirmed CD19 tumor expression; **AND**
IV. Individual has morphological disease in the bone marrow (greater than or equal to 5% blasts); **AND**
V. Individual has relapsed or refractory disease defined by any of the following:
    A. First relapse if first remission is greater than or equal to 12 months; **OR**
    B. Bone marrow relapse after allogeneic stem cell transplant; **OR**
    C. Primary refractory disease; **OR**
    D. Chemo-refractory after 2 or more lines of systemic therapy; **AND**
VI. If individual has Philadelphia chromosome positive (Ph+) ALL, confirmation of trial and inadequate response or intolerance to at least two tyrosine kinase inhibitor (TKI) therapies, or TKI therapy is contraindicated; **AND**
VII. Individual has adequate renal, hepatic, pulmonary, and cardiac function defined as:
    A. Creatinine clearance (as estimated by Cockcroft Gault) ≥ 60 cc/min; **AND**
    B. Serum alanine aminotransferase (ALT)/aspartate aminotransferase (AST) ≤ 2.5 x upper limit of normal (ULN); **AND**
    C. Total bilirubin ≤ 1.5 mg/dl, except in individuals with Gilbert's syndrome; **AND**
    D. Cardiac ejection fraction ≥ 50%, no evidence of pericardial effusion, and no clinically significant arrhythmias; **AND**
VIII. If previously treated with blinatumomab, individual has CD19 tumor expression in bone marrow or peripheral blood; **AND**
IX. Individual has not received prior treatment with CAR T-cell therapy or other genetically modified T-cell therapy; **AND**
X. Individual has an ECOG performance status of 0-1; **AND**
XI. Individual is using as a one-time, single administration treatment.

Tecartus (brexucabtagene autoleucel) for B-cell acute lymphoblastic leukemia (ALL) may not be approved for the following (NCT02614066):

I. Repeat administration; **OR**
II. Using in combination with other chemotherapy agents; **OR**
III. If prescribed in combination with other CAR T-cell immunotherapy (e.g. Abecma, Breyanzi, Carvykti, Kymriah, Yescarta); **OR**
IV. Individual has active GVHD; **OR**
V. Presence of CNS-3 disease or CNS-2 disease with neurological changes; **OR**

VI. History or presence of any CNS disorder such as a seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, or any autoimmune disease with CNS involvement; **OR**
VII. Diagnosis of Burkitt's lymphoma/leukemia; **OR**
VIII. Diagnosis of chronic myelogenous leukemia blast crisis; **OR**
IX. History of concomitant genetic syndrome such as Fanconi anemia, Kostmann syndrome, Shwachman-Diamond syndrome or any other known bone marrow failure syndrome; **OR**
X. History of chimeric antigen receptor therapy or other genetically modified T-cell therapy; **OR**
XI. Active or latent hepatitis B, active hepatitis C, human immunodeficiency virus (HIV) positive, or other active, uncontrolled infection; **OR**
XII. History of autoimmune disease (e.g. Crohns, rheumatoid arthritis, systemic lupus) resulting in end organ injury or requiring systemic immunosuppression/systemic disease modifying agents within the last 2 years; **OR**
XIII. When the above criteria are not met, and for all other indications.

Requests for Tecartus (brexucabtagene autoleucel) for **mantle cell lymphoma (MCL)** may be approved if the following criteria are met (Label, NCCN 2A):

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 renal, hepatic, pulmonary, and cardiac function defined as (Wang 2020):
  A. Creatinine clearance (as estimated by Cockcroft Gault) ≥ 60 cc/min; **AND**
  B. Serum alanine aminotransferase (ALT)/aspartate aminotransferase (AST) ≤ 2.5 x upper limit of normal (ULN); **AND**
  C. Total bilirubin ≤ 1.5 mg/dl, except in individuals with Gilbert's syndrome; **AND**
  D. Cardiac ejection fraction ≥ 50%, no evidence of pericardial effusion, and no clinically significant arrhythmias; **AND**
VII. 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**
VIII. Individual has a current ECOG performance status of 0-1 (Wang 2020); **AND**
IX. If individual has a history of an allogeneic stem cell transplant, there are no current signs of active graft versus host disease (GVHD); **AND**
X. Individual has not received prior treatment with CAR T cell therapy or other genetically modified T-cell therapy; **AND**
XI. Individual is using as a one-time, single administration treatment.

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

I. Repeat administration; **OR**
II. If prescribed in combination with other CAR T-cell immunotherapy (e.g. Abecma, Breyanzi, Carvykti, Kymriah, Yescarta); **OR**
III. Evidence of pericardial effusion as determined by an echocardiogram (ECHO), or other significant ECHO findings; **OR**
IV. History of a seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, cerebral edema, or posterior reversible encephalopathy syndrome; **OR**
V. Any autoimmune disease with central nervous system (CNS) involvement; **OR**
VI. Active or latent hepatitis B, active hepatitis C, human immunodeficiency virus (HIV) positive, or other active, uncontrolled infection; **OR**
VII. Using in combination with other chemotherapy agents (not including the use of lymphodepleting chemotherapy as labeled prior to Tecartus infusion); **OR**
VIII. Individual has active GVHD; **OR**
IX. 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.

CPT	
38225	Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day [Tecartus]
38226	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (eg, cryopreservation, storage) [Tecartus]
38227	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration [Tecartus]
38228	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous [Tecartus]
HCPCS	
Q2053	Brexucabtagene autoleucel, up to 200 million autologous anti-CD19 CAR positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
ICD-10 Procedure	
XW033M7	Introduction of brexucabtagene autoleucel immunotherapy into peripheral vein, percutaneous approach, new technology group 7 [Tecartus]
XW043M7	Introduction of brexucabtagene autoleucel immunotherapy into central vein, percutaneous approach, new technology group 7 [Tecartus]
ICD-10 Diagnosis	
C83.10-C83.19	Mantle cell lymphoma
C91.00-C91.02	Acute lymphoblastic leukemia
Z51.12	Encounter for antineoplastic immunotherapy

Document History

Reviewed: 11/15/2024
Document History:

- 12/17/2024 – Coding update only: Removed CPT codes 0537T, 0538T, 0539T, 0540T effective 12/31/24. Added CPT codes 38225, 38226, 38227, 38228 effective 1/1/25.
- 11/15/2024 – Annual Review: No criteria changes. Added references. Coding reviewed: Added CPT codes 0537T, 0538T, 0539T, 0540T. Added ICD-10-CM Z51.12.
- 09/18/2024 – Coding Reviewed: Added ICD-10 PCS codes XW033M7 and XW043M7.
- 11/19/2023 – Annual Review: For Mantle cell lymphoma, updated criteria to state “current signs of active graft vs host disease.” Coding Reviewed: No changes.
- 11/18/2022 – Annual Review: For B-cell ALL: Update criteria to include CD19 expression for diagnosis of B-cell ALL, Add criteria for prior CAR -T cell therapy individuals; Add to the may not be approved criteria for combination use with other CAR T- cell therapy and individuals with active GVHD. For Mantle Cell Lymphoma: Add criteria for lab values; Add criteria for history of allogeneic stem cell transplant; Add criteria for prior CAR -T cell therapy; Add to the may not be approved criteria for combination use with other CAR T- cell therapy and active GVHD; Removed duplicative criteria. Coding Reviewed: No changes.
- 12/13/2021 – Select Review: Update criteria to remove requirement for baseline oxygen saturation. Coding Reviewed: No changes.
- 11/19/2021 – Annual Review: Update criteria to add indication for B-cell acute lymphoblastic leukemia (ALL). Wording and formatting updates. Coding reviewed: Added ICD-10-CM C91.00-C91.02.
- 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. Effective 1/1/2021 Added HCPCS C9073, Removed HCPCS J3490, J3590. Added ICD-10-CM C83.10-C83.19 (Mantle Cell Lymphoma). Effective 4/1/2021- Added HCPCS Q2053. Removed HCPCS J9999, C9073.

References

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2024. URL: http://www.clinicalpharmacology.com. Updated periodically.
2. Common Terminology Criteria for Adverse Events (CTCAE), V5.0. Revised November 2017. National Institutes of Health, National Cancer Institute (NCI). Available at: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf.
3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: October 9, 2024.
4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
5. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2024; Updated periodically.

6. National Institutes of Health (NIH). Mantle Cell Lymphoma. Gaithersburg, MD. 2016. Available at https://rarediseases.info.nih.gov/diseases/6969/mantle-cell-lymphoma. Accessed on October 9, 2024.
7. NCCN Clinical Practice Guidelines in Oncology™. © 2024 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on October 9, 2024.
    a. B-Cell Lymphomas. V3.2024. Revised August 26, 2024.
    b. Acute Lymphomblastic Leukemia. V2.2024. Revised July 19, 2024.
8. NCT02601313. ClinicalTrials.gov. U.S. National Library of Medicine. Available at https://clinicaltrials.gov/ct2/show/NCT02601313?term=nct02601313&draw=2&rank=1.
9. NCT02614066. ClinicalTrials.gov. U.S National Library of Medicine, National Institutes of Health website. Available at https://clinicaltrials.gov/ct2/show/NCT02614066?term=brexucabtagene&draw=2&rank=4.
10. Shah B. Phase 2 results of the Zuma-3 study evaluating KTE-X19, an anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, in adult patients (pts) with relapsed/refractory B-cell acute lymphoblastic leukemia (R/R B-ALL) [abstract]. 2021 American Society of Clinical Oncology Annual Meeting. *J Clin Oncol*. 2021;39(suppl 15; abstr 7002). DOI: 10.1200/JCO.2021.39.15_suppl.7002 Available at: https://meetings.asco.org/abstracts-presentations/195802.
11. Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-Cell therapy in relapsed or refractory mantle-cell lymphoma. *N Eng J Med.* 2020;382:1331-42. Available at: https://www.nejm.org/doi/pdf/10.1056/NEJMoa1914347?articleTools=true.
12. 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. Available at: https://www.nejm.org/doi/suppl/10.1056/NEJMoa1914347/suppl_file/nejmoa1914347_appendix.pdf.

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.