Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Brexucabtagene autoleucel (Tecartus®)	MP-RX-FP-115-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drug

Service Description

This document addresses the use of Brexucabtagene autoleucel (Tecartus®), a CD19-directed genetically modified autologous T cell immunotherapy approved by the Food and Drug Administration (FDA) for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) and relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

Background Information

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 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.

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Approved Indications

Tecartus FDA-approved indications include:

- 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.
- Adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

Other Uses

None

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
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	Description
C83.10-C83.19	Mantle cell lymphoma
C91.00-C91.02	Acute lymphoblastic leukemia

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Medical Necessity Guidelines

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.

Brexucabtagene autoleucel (Tecartus®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

Requests for Tecartus (brexucabtagene autoleucel) for B-cell acute lymphoblastic leukemia (ALL) may be approved if the following criteria are met (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.

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Requests for Tecartus (brexucabtagene autoleucel) for **mantle cell lymphoma (MCL)** 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 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 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.

B. Criteria For Continuation of Therapy

i. Further treatment with Tecartus will not be authorized since it is designated for a single-dose administration as per its indication.

C. Authorization Duration

i. Initial Approval Duration: 3 months (1 dose only, tocilizumab (Actemra) will be approved if requested)

ii. Reauthorization Approval Duration: Not applicable

D. **Conditions Not Covered**

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

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. Crohn's, 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 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**

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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.

Limits or Restrictions

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

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Drug	Recommended Dosing Schedule
Relapsed or refractory Mantle Cell Lymphoma (MCL)	The target dose is 2 × 106 CAR-positive viable T cells per kg body weight, with a maximum of 2 × 108 CAR- positive viable T cells.
Acute Lymphoblastic Leukemia (ALL)	The target dose is 1 × 106 CAR-positive viable T cells per kg body weight, with a maximum of 1 × 108 CAR- positive viable T cells.

Additional Dosing Information

- Tecartus is designated for autologous administration via intravenous infusion solely within a certified healthcare setting.
- **Pretreatment**:
  - MCL: Tecartus should be initiated 2 days after completing lymphodepleting chemotherapy regimen with cyclophosphamide 500 mg/m^2/day intravenously (IV) and fludarabine 30 mg/m^2/day IV for 3 days.
  - ALL: Tecartus should be initiated 1 day after completing lymphodepleting chemotherapy regimen with fludarabine 25 mg/m^2/day IV for 3 days. Cyclophosphamide 900 mg/m^2 should be administered one day prior to administering Tecartus.
- **Premedication** should include acetaminophen and diphenhydramine (or another H1-antihistamine) approximately 30 to 60 minutes before infusion of Tecartus. Prophylactic use of systemic corticosteroids should be avoided, as the use may interfere with the activity of Tecartus.
- **Post-medication**: Tocilizumab plays an important role in the treatment of patients receiving CAR T-cell therapy such as Tecartus. It manages and mitigates cytokine release syndrome (CRS), which can occur after CAR T-cell infusion. Tocilizumab should be available to the patient prior to infusion and during the recovery period.

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Reference Information

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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.

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Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Inception	Adopted From Elevance	N/A	12/22/2023
Select Review	Update statement for criteria for initial approval: Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met all approval criteria.	Click or tap to enter a date.	Click or tap to enter a date.

Revised: 11/30/2023