Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 02/01/2022**
Policy Number: PA.CP.PHAR.472	**Effective Date: 08/2020** **Revision Date: 01/2022**
Policy Name: Brexucabtagene Autoleucel (Tecartus)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

1Q 2022 annual review: ALL – criteria updated per FDA labeling; added additional requirements for CNS disease exclusions per ZUMA-3 clinical trial exclusion criteria; coding information added; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

Clinical Policy: Brexucabtagene Autoleucel (Tecartus)

Reference Number: PA.CP.PHAR.472
Effective Date: 08/2020
Last Review Date: 01/2022

Coding Implications
Revision Log

Description
Brexucabtagene autoleucel (Tecartus®) is a CD19-directed chimeric antigen receptor (CAR) T cell therapy.

FDA Approved Indication(s)
Tecartus is 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.*

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness® that Tecartus is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Mantle Cell Lymphoma* (must meet all)**:**

**Only for initial treatment dose; subsequent doses will not be covered.*

1. Diagnosis of relapsed or refractory MCL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Recent (within the last 30 days) absolute lymphocyte count (ALC) ≥ 100 cells/µL;
5. Member has previously received 2 to 5 prior regimens that included all of the following (a, b, and c):
   a. Anthracycline (e.g., doxorubicin) or bendamustine-containing chemotherapy;
   b. Anti-CD20 monoclonal antibody therapy (e.g., rituximab);
   c. Bruton tyrosine kinase (BTK) inhibitor (e.g., Imbruvica®, Calquence®, Brukinsa™);
6. Member does not have a history of or current central nervous system (CNS) disease or CNS disorders as detected by magnetic resonance imaging [MRI] (i.e., detectable cerebrospinal fluid malignant cells or brain metastases, CNS lymphoma, seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, cerebral edema, posterior reversible encephalopathy syndrome, or any autoimmune disease with CNS involvement);
7. Member does not have a history of allogeneic stem cell transplantation;
8. Member has not previously received treatment with CAR T-cell immunotherapy (e.g., Abecma, Breyanzi, Kymriah, Yescarta);

9. Tecartus is not prescribed concurrently with other CAR T-cell immunotherapy (e.g., Abecma, Breyanzi, Kymriah, Yescarta);
10. Dose does not exceed 2 x 10^8 CAR-positive viable T cells

Approval duration: 3 months ***(1 dose only, with 4 doses of tocilizumab (Actemra) at up to 800 mg per dose)***

B. Acute Lymphoblastic Leukemia* (must meet all):
**Only for initial treatment dose; subsequent doses will not be covered.*

1. Diagnosis of B-cell precursor ALL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Recent (within the last 30 days) ALC ≥ 100/µL;
5. Request meets one of the following (a or b):
   a. Member has relapsed or refractory disease defined as one of the following (i - iv):
      i. Primary refractory disease;
      ii. First relapse if first remission ≤ 12 months;
      iii. Relapsed or refractory disease after 2 or more lines of systemic therapy;
      iv. Relapsed following allogeneic stem cell transplantation (allo-SCT) and must be ≥ 100 days from allo-SCT at the time of Tecartus infusion;
   b. Disease is Philadelphia chromosome positive, and failure of 2 tyrosine kinase inhibitors (e.g., imatinib, Sprycel®, Tasigna®, Bosulif®, Iclusig®) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
      **Prior authorization may be required for tyrosine kinase inhibitors*
6. If previously treated with Blincyto®, documentation of CD19 tumor expression on blasts obtained from bone marrow or peripheral blood after completion of the most recent prior line of therapy;
7. Member does not have CNS-3 disease* or have a history or presence of any CNS disorder (e.g., seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, any autoimmune disease with CNS involvement, posterior reversible encephalopathy syndrome, or cerebral edema);
   **CNS-3 disease is defined as detectable cerebrospinal blast cells in a sample of CSF with ≥ 5 white blood cells (WBCs) per mm^3*
8. If member has CNS-2 disease*, documentation of no clinically evident neurological changes;
   **CNS-2 disease is defined as CSF blast cells with < 5 WBC/mm^3*
9. Member has not previously received treatment with CAR T-cell immunotherapy (e.g., Abecma, Breyanzi, Kymriah, Yescarta);
10. Tecartus is not prescribed concurrently with other CAR T-cell immunotherapy (e.g., Abecma, Breyanzi, Kymriah, Yescarta);
11. Dose does not exceed 1 x 10^8 CAR-positive viable T cells.

Approval duration: 3 months ***(1 dose only, with 4 doses of tocilizumab (Actemra) if requested at up to 800 mg per dose)***

C. Other diagnoses/indications

Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. All Indications in Section I

1. Continued therapy will not be authorized as Tecartus is indicated to be dosed one time only.

Approval duration: Not applicable

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53;

B. MCL: History of or current CNS disease or CNS disorders as detected by MRI (i.e., detectable cerebrospinal fluid malignant cells or brain metastases, CNS lymphoma, seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, cerebral edema, posterior reversible encephalopathy syndrome, or any autoimmune disease with CNS involvement);

C. MCL: History of allo-SCT;

D. ALL: History or presence of any CNS disorder, such as a seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, any autoimmune disease with CNS involvement, posterior reversible encephalopathy syndrome, or cerebral edema;

E. ALL: Presence of CNS-3 disease defined as detectable cerebrospinal blast cells in a sample of CSF with ≥ 5 white blood cells (WBCs) per mm^3 with or without neurological changes.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALC: absolute lymphocyte count
Allo-SCT: allogeneic stem cell transplantation
ALL: acute lymphoblastic leukemia
CAR: chimeric antigen receptor
CNS: central nervous system
CSF: cerebrospinal fluid
FDA: Food and Drug Administration
MCL: mantle cell lymphoma
MRI: magnetic resonance imaging
WBC: white blood cells

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone/methotrexate/ cytarabine) + rituximab	Varies	Varies
NORDIC (rituximab + cyclophosphamide, vincristine, doxorubicin, prednisone/rituximab + cytarabine)	Varies	Varies
RCHOP/RDHAP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)/(rituximab, dexamethasone, cisplatin, cytarabine)	Varies	Varies
RDHA (rituximab, dexamethasone, cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin)	Varies	Varies
RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
Bendeka® (bendamustine) ± rituximab	Varies	Varies
VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)	Varies	Varies
Revlimid® (lenalidomide) + rituximab	Varies	Varies
bortezomib ± rituximab	Varies	Varies
lenalidomide ± rituximab	Varies	Varies
Imbruvica® (ibrutinib) ± rituximab	560 mg PO QD	560 mg/day
Calquence® (acalabrutinib)	100 mg PO BID	400 mg/day
Brukinsa® (zanubrutinib)	160 mg PO BID or 320 mg PO QD	320 mg/day
Venclexta® (venetoclax)	20 mg/day for week 1, 50 mg/day for week 2, 100 mg/day for week 3, 200 mg/day for week 4, 400 mg/day for week 5. Week 6 and thereafter: 800 mg/day	800 mg/day
Acute Lymphoblastic Leukemia		
imatinib mesylate (Gleevec®)	Adults with Ph+ ALL: 600 mg/day Pediatrics with Ph+ ALL: 340 mg/m^2/day	Adults: 800 mg/day Pediatrics: 600 mg/day
Sprycel® (dasatinib)	Ph+ ALL: 140 mg per day	180 mg/day
Iclusig® (ponatinib)	Ph+ ALL: 45 mg per day	45 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Tasigna® (nilotinib)	Resistant or intolerant Ph+ CML-CP and CML-AP: 400 mg twice per day	800 mg/day
Bosulif® (bosutinib)	Ph+ CML: 500 mg per day	600 mg/day
Various combination regimens that may include the following: daunorubicin, doxorubicin, vincristine, dexamethasone, prednisone, pegaspargase, nelarabine, methotrexate, cyclophosphamide, cytarabine, rituximab, 6-mercaptopurine	Ph- ALL: varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s):
  - Cytokine release syndrome: do not administer Tecartus to patients with active infection or inflammatory disorders; treat severe or life-threatening cytokine release syndrome with tocilizumab or tocilizumab and corticosteroids
  - Neurologic toxicities: monitor for neurologic toxicities after treatment with Tecartus; provide supportive care and/or corticosteroids, as needed

Appendix D: General Information

- The ZUMA-2 trial included only patients with an ALC ≥ 100 cells/µL and a magnetic resonance imaging (MRI) of the brain showing no evidence of CNS lymphoma. Subjects with detectable cerebrospinal fluid malignant cells or brain metastases or with a history of CNS lymphoma were excluded. The trial also excluded patients with history or presence of CNS disorder, such as seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, cerebral edema, posterior reversible encephalopathy syndrome, or any autoimmune disease with CNS involvement. Additionally patients with a history of allogeneic stem cell transplantation or prior CAR therapy or other genetically modified T-cell therapy were excluded.
- Tecartus is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Yescarta and Tecartus REMS Program.
- Refractory disease is defined as an inability to achieve a complete response to therapy.
- The ZUMA-3 trial in patients with ALL excluded patients with:
  - Presence of CNS-3 disease defined as detectable cerebrospinal blast cells in a sample of CSF with ≥ 5 WBCs per mm^3 with or without neurological changes;
  - Presence of CNS-2 disease defined as detectable cerebrospinal blast cells in a sample of CSF with <5 WBCs per mm^3 with neurological changes;

- History or presence of any CNS disorder, such as a seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, any autoimmune disease with CNS involvement, posterior reversible encephalopathy syndrome, or cerebral edema.
-

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MCL	Target dose: 2×10^6 CAR-positive viable T cells per kg body weight	2×10^8 CAR-positive viable T cells
ALL	1×10^6 CAR-positive viable T cells/kg	1×10^8 CAR-positive viable T cells/kg

VI. Product Availability

Single-dose unit infusion bag: frozen suspension of genetically modified autologous T-cells labeled for the specific recipient

VII. References

1. Tecartus Prescribing Information. Santa Monica, CA: Kite Pharma, Inc.; October 2021. Available at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/tecartus/tecartus-pi.pdf. Accessed October 18, 2021.
2. Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. N Engl J Med 2020;382:1331-42.
3. National Comprehensive Cancer Network. B-cell Lymphomas Version 5.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed October 18, 2021.
4. Shah BD, Ghobadi A, Oluwole OO, et al. KTE-X19 for relapsed or refractory adult B-cell acute lymphoblastic leukaemia: phase 2 results of the single-arm, open-label, multicentre ZUMA-3 study. Lancet. 2021 Jun 3; S0140-6736 (21) 01222-8.
5. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed October 18, 2021.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9073	Suspension C9073 Brexucabtagene autoleucel, up to 200 million autologous anti-cd19 car positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2053	Brexucabtagene autoleucel, up to 200 million autologous anti-cd19 car positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose

Reviews, Revisions, and Approvals	Date
Policy created	09/2020
1Q 2021 annual review: clarified CNS disease should be ruled out by MRI; references reviewed and updated.	01/2021
1Q 2022 annual review: ALL – criteria updated per FDA labeling; added additional requirements for CNS disease exclusions per ZUMA-3 clinical trial exclusion criteria; coding information added; references reviewed and updated.	01/2022