# Clinical Policy: Brexucabtagene Autoleucel (Tecartus)

Reference Number: ERX.SPA.380
Effective Date: 07.24.20
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**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)*
- **[Pending]** Adult patients with relapsed or refractory B-cell precursor acute lymphoblastic lymphoma (ALL)

**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.*

*Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.*

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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., Kymriah™, Yescarta™);
9. Tecartus is not prescribed concurrently with other CAR T-cell immunotherapy (e.g., Kymriah, Yescarta);
10. Dose does not exceed 2 x $10^8$ CAR-positive viable T cells/kg.

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

**B. Acute Lymphoblastic Leukemia*** (must meet all):
**Criteria will mirror the clinical information from the prescribing information once FDA-approved*
**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. If member has CNS-2 disease*, documentation of no clinically evident neurological changes;*
   **CNS-2 disease is defined as cerebrospinal fluid blast cells with < 5 white blood cells/$mm^3$*
8. Member has not previously received treatment with CAR T-cell immunotherapy (e.g., Kymriah, Yescarta);
9. Tecartus is not prescribed concurrently with other CAR T-cell immunotherapy (e.g., Kymriah, Yescarta);
10. Dose does not exceed one of the following (a or b):*
    a. Weight ≤ 100 kg: 1 x $10^6$ CAR-positive viable T cells/kg;
    b. Weight > 100 kg: 1 x $10^8$ CAR-positive viable T cells/kg.

**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**
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

## 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 ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

## 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 – ERX.PA.01 or evidence of coverage documents;

**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.

## 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
FDA: Food and Drug Administration
MCL: mantle cell lymphoma
MRI: magnetic resonance imaging

*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 and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| **Mantle Cell Lymphoma** | | |
| 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<br>Pediatrics with Ph+ ALL: 340 mg/m$^2$/day | Adults: 800 mg/day<br>Pediatrics: 600 mg/day |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| Sprycel® (dasatinib) | Ph+ ALL: 140 mg per day | 180 mg/day |
| Iclusig® (ponatinib) | Ph+ ALL: 45 mg per day | 45 mg/day |
| 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/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.

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| MCL | Target dose: $2 \times 10^6$ CAR-positive viable T cells per kg body weight | $2 \times 10^8$ CAR-positive viable T cells |
| ALL* | Weight ≤ 100 kg: $1 \times 10^6$ CAR-positive viable T cells/kg*<br><br>Weight > 100 kg: $1 \times 10^8$ CAR-positive viable T cells/kg* | See dosing regimen |

## 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.; July 2020. Available at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/tecartus/tecartus-pi.pdf. Accessed November 18, 2020.
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 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed November 18, 2020.
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.

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| Policy created pre-emptively | 02.26.20 | 05.20 |
| Drug is now FDA approved - criteria updated per FDA labeling as an RT1: clarified excluded use to include other CNS disorders and history of allogeneic stem cell transplant per clinical trial exclusion criteria; clarified requirement of 2 to 5 prior regimens; added requirement for baseline ALC ≥ 100/µL per clinical trial inclusion criteria; updated target and maximum dosing per prescribing information; added Actemra maximum doses for cytokine release syndrome to approval duration; references reviewed and updated. | 07.27.20 | 11.20 |
| 1Q 2021 annual review: clarified CNS disease should be ruled out by MRI; references reviewed and updated. | 11.18.20 | 02.21 |
| Added preemptive criteria for the pending FDA approval of ALL indication; clarified Actemra authorization may be considered if requested. | 06.08.21 | 08.21 |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.