Brexucabtagene Autoleucel (Tecartus)

Number: 0980

POLICY

Note: Requires Precertification.

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.

Precertification of brexucabtagene autoleucel (Tecartus) is required of all Aetna participating providers and members in applicable plan designs. For precertification of brexucabtagene autoleucel (Tecartus), call 1-877-212-8811.

I. Criteria for Initial Approval

A. Mantle Cell Lymphoma

Aetna considers brexucabtagene autoleucel (Tecartus) medically necessary for treatment of mantle cell lymphoma in members 18 years of age or older when all of the following criteria are met:

1. The disease is relapsed or refractory; and
2. The member has had previous treatment with both chemoimmunotherapy and a bruton tyrosine kinase inhibitor (e.g., ibrutinib); and
3. The member has not received a previous treatment course of brexucabtagene autoleucel or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy; and
4. The member has an ECOG performance status of 0 to 2 (See Appendix); and
5. The member has adequate and stable kidney, liver, pulmonary and cardiac function; and
6. The member does not have active hepatitis B, active hepatitis C or any active uncontrolled infection; and
7. The member does not have an active inflammatory disorder

B. Adult Relapsed or Refractory B-cell precursor Acute Lymphoblastic Leukemia (ALL)

Aetna considers brexucabtagene autoleucel (Tecartus) medically necessary for treatment of B-cell precursor acute lymphoblastic leukemia (ALL) in members 18 years of age or older when all of the following criteria are met:

1. The member has not received a previous treatment course of the requested medication or another CD19-directed chimeric antigen receptor (CAR-T) therapy, or any prior CD19 directed therapy other than blinatumomab; and

2. The member meets either of the following criteria:
   a. Member has Philadelphia chromosome-negative disease that is relapsed or refractory as defined as one of the following:
      i. Primary refractory disease; or
      ii. First relapse with remission of 12 months or less; or
      iii. Relapsed or refractory disease after at least 2 previous lines of systemic therapy; or
      iv. Relapsed or refractory disease after allogeneic stem cell transplant (allo-SCT); or

   b. Member has Philadelphia chromosome-positive disease and meets any of the following:
      i. The member has relapsed or refractory disease despite treatment with at least 2 different tyrosine kinase inhibitors (TKIs) (e.g., bosutinib, dasatinib, imatinib, nilotinib, ponatinib); or
      ii. The member is intolerant to TKI therapy
3. The member has morphological disease in the bone marrow (>5% blasts); and
4. The member has an ECOG performance status of 0 to 2 (See Appendix); and
5. The member has adequate and stable kidney, liver, pulmonary, and cardiac function; and
6. The member does not have active hepatitis B, active hepatitis C, or any active uncontrolled infection; and
7. The member does not have active graft versus host disease; and
8. The member does not have an active inflammatory disorder.

Aetna considers all other indications as experimental and investigational.

II. Continuation of Therapy

See Dosage and Administration information.

Dosage and Administration

Brexucabtagene autoleucel (Tecartus) is available as a cell suspension for autologous and for intravenous use only.

Dosing of Tecartus is based on the number of chimeric antigen receptor (CAR)-positive viable T cells. Each single infusion bag of Tecartus contains a suspension of chimeric antigen receptor (CAR)-positive T cells in approximately 68 mL Brexucabtagene autoleucel (Tecartus) should be administered in a certified healthcare facility.

*Mantle cell lymphoma:*

The target dose is $2 \times 10^6$ CAR-positive viable T cells per kg body weight, with a maximum of $2 \times 10^8$ CAR-positive viable T cells.

*Acute lymphoblastic leukemia:*

The target dose is $1 \times 10^6$ CAR-positive viable T cells per kg body weight, with a maximum of $1 \times 10^8$ CAR-positive viable T cells.

Source: Kite Pharma, 2021
BACKGROUND

U.S. Food and Drug Administration (FDA)-Approved Indications

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

Brexucabtagene autoleucel is available as Tecartus (Kite Pharma, Inc.) and is a CD19-directed genetically modified autologous T cell immunotherapy. Brexucabtagene autoleucel (Tecartus) binds to CD19-expressing cancer cells and normal B cells. Additionally, the CD28 and CD3-zeta co-stimulatory domains activate downstream signaling cascades that direct T cell activation, proliferation, acquisition of effector functions, and secretion of inflammatory cytokines and chemokines. This chain of events leads to killing of CD19-expressing cells (Kite Pharma, 2021).

Per the prescribing information, brexucabtagene autoleucel (Tecartus) carries the following black box warnings:

- Cytokine release syndrome (CRS): CRS, including life-threatening reactions, have been noted after treatment with Tecartus. In the ZUMA-2 study, CRS occurred in 91% (75/82) of patients receiving Tecartus, including ≥ grade 3 CRS in 18% of patients. One patient had a fatal CRS event.
- Neurologic toxicities: Neurologic events, including those that were life-threatening, have been noted after treatment with Tecartus. In the ZUMA-2 study, neurologic events occurred in 81% of patients, 37% of whom noted grade 3 or higher (severe or life-threatening) adverse reactions.

Additional warnings and precautions per the prescribing information include hypersensitivity reactions, severe infections, prolonged cytopenias, hypogammaglobulinemia, secondary malignancies, and effects on ability to drive and use machines.

The most common non-laboratory adverse reactions (occurrence ≥ 20%) per the prescribing information include pyrexia, CRS, hypotension,
encephalopathy, fatigue, tachycardia, arrhythmia, infection - pathogen unsuspected, chills, hypoxia, cough, tremor, musculoskeletal pain, headache, nausea, edema, motor dysfunction, constipation, diarrhea, decreased appetite, dyspnea, rash, insomnia, pleural effusion, and aphasia.

**Mantle Cell Lymphoma**

On July 24, 2020, the FDA approved a chimeric antigen receptor (CAR) T-cell therapy, Tecartus (brexucabtagene autoleucel), for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL). The approval of brexucabtagene autoleucel (KTE-X19), is based on efficacy and safety data from the ongoing, single-arm, open-label, multicenter trial (ZUMA-2; NCT02601313), which evaluated the efficacy and safety of a single infusion in adult patients with relapsed or refractory mantle cell lymphoma (MCL) who had previously received anthracycline- or bendamustine-containing chemotherapy, an anti-CD20 antibody, and a Bruton tyrosine kinase inhibitor (BTKi; ibrutinib or acalabrutinib). The study excluded patients with active or serious infections, prior allogeneic hematopoietic stem cell transplant (HSCT), detectable cerebrospinal fluid malignant cells or brain metastases, and any history of central nervous system (CNS) lymphoma or CNS disorders (FDA 2020).

Seventy-four patients were leukapheresed, five (7%) of whom did not begin conditioning chemotherapy or receive brexucabtagene autoleucel: three (4%) experienced manufacturing failure, one (1%) died of progressive disease, and one (1%) withdrew from the study. One patient (1%) received lymphodepleting chemotherapy but did not receive brexucabtagene autoleucel due to ongoing active atrial fibrillation. Sixty-eight of the patients who were leukapheresed received a single infusion of brexucabtagene autoleucel, and 60 of these patients were followed for at least six months after their first objective disease response, qualifying them as efficacy-evaluable. Among the 60 efficacy-evaluable patients, $2 \times 10^6$ CAR-positive viable T cells/kg were administered to 54 (90%). The remaining six (10%) patients received doses of 1.0, 1.6, 1.8, 1.8, 1.9, and $1.9 \times 10^6$ CAR-positive viable T cells/kg. Of the 60 efficacy-evaluable patients, the median age was 65 years (range: 38 to 79 years), 51 (85%) were male, and 56 (93%) were white. Most (50 patients; 83%) had stage IV disease. Twenty patients (33% of 60) had baseline bone marrow examinations performed per protocol; of these, ten (50%) were negative, eight (40%) were positive, and two (10%) were indeterminate. The
median number of prior therapies among all 60 efficacy-evaluable patients was three (range: two to five). Twenty-six (43%) of the patients had relapsed after or were refractory to autologous HSCT. Twenty-one (35%) had relapsed after their last therapy for MCL, while 36 (60%) were refractory to their last therapy for MCL. Among the 60 efficacy-evaluable patients, 14 (23%) had blastoid MCL. Following leukapheresis and prior to administration of brexucabtagene autoleucel, 21 (35%) of the 60 patients received bridging therapy. Sixteen (27%) were treated with a BTKi, 9 (15%) with a corticosteroid, and 4 (7%) with both a BTKi and a corticosteroid. Among the 60 efficacy-evaluable patients, the median time from leukapheresis to product delivery was 15 days (range: 11 to 28 days), and the median time from leukapheresis to product infusion was 27 days (range: 19 to 63 days). The protocol-defined lymphodepleting chemotherapy regimen of cyclophosphamide 500 mg/m² intravenously and fludarabine 30 mg/m² intravenously, both given on each of the fifth, fourth, and third days before brexucabtagene autoleucel infusion, was administered to 53 (88%) of the 60 efficacy-evaluable patients. The remaining seven patients (12%) either received lymphodepletion over four or more days or received brexucabtagene autoleucel four or more days after completing lymphodepletion. All treated patients received brexucabtagene autoleucel infusion on Day 0 and were hospitalized until at least Day 7 (Kite Pharma, 2020).

The primary endpoint was objective response rate (ORR) per the Lugano Classification (2014) in patients treated with brexucabtagene autoleucel as determined by an independent review committee. According to published study results, the primary efficacy analysis showed that 93% (95% confidence interval [CI], 84 to 98) of the 60 patients in the primary efficacy analysis had an objective response; 67% (95% CI, 53 to 78) had a complete response. In an intention-to-treat analysis involving all 74 patients, 85% had an objective response; 59% had a complete response. At a median follow-up of 12.3 months (range, 7.0 to 32.3), 57% of the 60 patients in the primary efficacy analysis were in remission. At 12 months, the estimated progression-free survival and overall survival were 61% and 83%, respectively (Wang 2020).
Acute Lymphoblastic Leukemia

On October 1, 2021, the United States Food and Drug Administration (FDA) granted approval for Tecartus (brexucabtagene autoleucel) for the treatment of adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). The FDA approval was subsequent to the FDA Breakthrough Therapy Designation and a priority review. Additionally, the basis of this approval was supported from the efficacy outcome measures in the pivotal phase 2 ZUMA-3 study (Kite, 2021).

Shah and colleagues (2021) evaluated the efficacy and safety of brexucabtagene autoleucel in adult patients with relapsed or refractory B-precursor acute lymphoblastic leukemia in the pivotal phase 2 ZUMA-3 study, an international, multicenter, single-arm, open-label study. Brexucabtagene autoleucel was successfully manufactured for 65 (92%) patients and administered to 55 (77%) patients with a median age of 40 years. The primary endpoint was the rate of overall complete remission or complete remission with hematological recovery. Secondary endpoints included: duration of remission and relapse-free survival, overall survival, minimal residual disease (MRD) negativity rate, and allogenic stem-cell transplant (allo-SCT) rate. At the median follow-up of 16.4 months (13.8-19.6), 39 patients (71%; 95% confidence interval [CI] 57-82, p<0.0001) had complete remission or complete remission with incomplete hematological recovery, with 31 (56%) patients reaching complete remission. Median duration of remission was 12.8 months (95% CI 8.7-not estimable), median relapse-free survival was 11.6 months (2.7-15.5), and median overall survival was 18.2 months (15.9-not estimable). Among responders, the median overall survival was not achieved, and 38 (97%) patients had MRD negativity. In addition, 10 (18%) patients received allo-SCT consolidation after brexucabtagene autoleucel infusion.

The most common adverse events of grade 3 or higher were anemia in 27 (49%) patients and pyrexia in 20 (36%) patients. Fourteen (25%) patients had infections of grade 3 or higher.
Table: ECOG Performance Status

<table>
<thead>
<tr>
<th>Grade</th>
<th>ECOG</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fully active, able to carry on all pre-disease performance without restriction</td>
</tr>
<tr>
<td>1</td>
<td>Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (e.g., light house work, office work)</td>
</tr>
<tr>
<td>2</td>
<td>Ambulatory and capable of all self-care but unable to carry out work activities. Up and about more than 50% of waking hours</td>
</tr>
<tr>
<td>3</td>
<td>Capable of only limited self-care, confined to bed or chair more than 50% of waking hours</td>
</tr>
<tr>
<td>4</td>
<td>Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair</td>
</tr>
<tr>
<td>5</td>
<td>Dead</td>
</tr>
</tbody>
</table>


CPT Codes/ HCPCS Codes/ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by “+”

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CPT codes covered if selection criteria are met:</td>
</tr>
<tr>
<td></td>
<td>Code Description</td>
</tr>
<tr>
<td>0537T</td>
<td>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</td>
</tr>
<tr>
<td>0538T</td>
<td>preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage)</td>
</tr>
<tr>
<td>0539T</td>
<td>receipt and preparation of CAR-T cells for administration</td>
</tr>
<tr>
<td>0540T</td>
<td>CAR-T cell administration, autologous</td>
</tr>
</tbody>
</table>

Other CPT codes related to the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>96413 - 96417</td>
<td>Intravenous chemotherapy administration</td>
</tr>
</tbody>
</table>

HCPCS codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q2053</td>
<td>Brexucabtagene autoleucel, up to 200 million autologous anti-cd19 car positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose</td>
</tr>
</tbody>
</table>
ICD-10 codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C83.10</td>
<td>Mantle cell lymphoma [relapsed or refractory]</td>
</tr>
<tr>
<td>C83.19</td>
<td></td>
</tr>
</tbody>
</table>

The above policy is based on the following references:

1. Kite. U.S. FDA approves Kite’s Tecartus as the first and only CAR T for adults with relapsed or refractory B-cell acute lymphoblastic leukemia. Press Release. Santa Monica, CA: Kite; October 1, 2021.


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: Brexucabtagene Autoleucel (Tecartus)

There are no amendments for Medicaid.

Revised 11/30/2021