Clinical Policy: Brexucabtagene Autoleucel (Tecartus)
Reference Number: CP.PHAR.472
Effective Date: 07.24.20
Last Review Date: 08.20
Line of Business: Commercial, HIM, Medicaid

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).*

*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 Centene Corporation® 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 (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 $2 \times 10^8$ CAR-positive viable T cells/kg.

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

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): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy
A. Mantle Cell Lymphoma
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): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and 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 – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
B. History of or current CNS disease or CNS disorders (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. History of allogeneic stem cell transplantation.

IV. Appendices/General Information
Appendix A: Abbreviation/Acronym Key
ALC: absolute lymphocyte count
CAR: chimeric antigen receptor
CNS: central nervous system
FDA: Food and Drug Administration
MCL: mantle cell lymphoma
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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone/methotrexate/cytarabine) + rituximab</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>NORDIC (rituximab + cyclophosphamide, vincristine, doxorubicin, prednisone/rituximab + cytarabine)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>RCHOP/RDHAP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)/(rituximab, dexamethasone, cisplatin, cytarabine)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>RDHA (rituximab, dexamethasone, cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Bendeka® (bendamustine) ± rituximab</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Revlimid® (lenalidomide) + rituximab</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>bortezomib ± rituximab</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>lenalidomide ± rituximab</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>Imbruvica® (ibrutinib) ± rituximab</td>
<td>560 mg PO QD</td>
<td>560 mg/day</td>
</tr>
<tr>
<td>Calquence® (acalabrutinib)</td>
<td>100 mg PO BID</td>
<td>400 mg/day</td>
</tr>
<tr>
<td>Brukinsa® (zanubrutinib)</td>
<td>160 mg PO BID or 320 mg PO QD</td>
<td>320 mg/day</td>
</tr>
<tr>
<td>Venclexta® (venetoclax)</td>
<td>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</td>
<td>800 mg/day</td>
</tr>
</tbody>
</table>

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.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCL</td>
<td>Target dose: 2 × 10⁶ CAR-positive viable T cells per kg body weight</td>
<td>2 × 10⁸ CAR-positive viable T cells</td>
</tr>
</tbody>
</table>

VI. Product Availability

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

VII. References


Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Policy created pre-emptively</td>
<td>02.26.20</td>
<td>05.20</td>
</tr>
<tr>
<td>Drug is now FDA approved - criteria updated per FDA labeling as an RT1:</td>
<td>07.27.20</td>
<td>08.20</td>
</tr>
<tr>
<td>clarified excluded use to include other CNS disorders and history of</td>
<td></td>
<td></td>
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<tr>
<td>allogeneic stem cell transplant per clinical trial exclusion criteria;</td>
<td></td>
<td></td>
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<tr>
<td>clarified requirement of 2 to 5 prior regimens; added requirement for</td>
<td></td>
<td></td>
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<tr>
<td>baseline ALC ≥ 100/μL per clinical trial inclusion</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Reviews, Revisions, and Approvals**

| Criteria; updated target and maximum dosing per prescribing information; added Actemra maximum doses for cytokine release syndrome to approval duration; references reviewed and updated. | Date | P&T Approval Date |

**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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.