

## Axicabtagene Ciloleucel

**NDC CODE(S)** 71287-0119-XX YESCARTA PLASTIC BAG, INJECTION (KITE PHARMA, IN)

### DESCRIPTION

Axicabtagene ciloleucel is a CD19-directed genetically modified autologous T cell immunotherapy. To prepare the product an individual's own T cells are harvested and genetically modified ex vivo by retroviral transduction to express a chimeric antigen receptor (CAR) comprising a murine anti-CD19 single chain variable fragment (scFv) linked to CD28 and CD3-zeta co-stimulatory domains. The anti-CD19 CAR T cells are expanded and infused back into the individual.

Axicabtagene ciloleucel binds to CD19-expressing cancer cells and normal B cells. Studies demonstrated that following anti-CD19 CAR T cell engagement with CD19-expressing target cells, the CD28 and CD3-zeta co-stimulatory domains activate downstream signaling cascades that lead to T-cell activation, proliferation, acquisition of effector functions and secretion of inflammatory cytokines and chemokines. This sequence of events leads to killing of CD19-expressing cells.

### POLICY

- Axicabtagene ciloleucel for the treatment of large B-cell lymphoma is considered **medically necessary** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Axicabtagene ciloleucel for the treatment of other conditions/diseases is considered **investigational**.

### MEDICAL APPROPRIATENESS

#### INITIAL APPROVAL

- **Submission of medical records related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation via direct upload through the PA web portal or by fax**
- Axicabtagene ciloleucel is considered **medically appropriate** if **ALL** of the following:
  - Individual is/has **ALL** of the following:
    - 18 years of age or older
    - Been screened for hepatitis B (HBV), Hepatitis C (HCV) and human immunodeficiency virus (HIV) in accordance with clinical guidelines prior to collection of cells (leukapheresis)
    - Not received live vaccines within 6 weeks prior to the start of lymphodepleting chemotherapy and during treatment with axicabtagene ciloleucel will not receive live vaccines until immune recovery following treatment
  - **Absence** of **ALL** of the following:
    - Clinically significant active systemic infection
    - Inflammatory disorders
    - Primary central nervous system lymphoma
    - Prior allogeneic hematopoietic stem cell transplantation
    - Prior CAR-T therapy
    - Prior anti-CD19 therapy, e.g., blinatumomab, etc., OR received anti-CD19 therapy and re-biopsy indicates CD-19 positive disease
    - Diagnosis of Primary Central Nervous System Lymphoma
  - Prophylaxis for infection has been followed according to local guidelines
  - Used as single agent therapy (not applicable to lymphodepleting or additional chemotherapy while awaiting manufacture)
  - Eastern Cooperative Oncology Group (ECOG) performance status is 0-1



- Treating healthcare facility is enrolled in the Yescarta **and Tecartus** REMS program and providers are trained in the management of cytokine release syndrome and neurological toxicities
- Individual is diagnosed with Large B-Cell Lymphoma that is relapsed or refractory, defined as a relapse within 1 year after autologous hematopoietic stem cell transplantation (HSCT) **OR** disease refractory to the most recent therapy and is further diagnosed as **ANY ONE** of the following:
  - Diffuse Large B-cell Lymphoma (DLBCL) as histologic transformation if individual received two or more prior lines of systemic therapy which must have included an anthracycline or anthracenedione-based regimen, unless contraindicated with transformation from **ANY ONE** of the following:
    - Follicular Lymphoma (FL) **or Nodal Marginal Zone Lymphoma after multiple lines of prior therapies for indolent or transformed disease**
    - Follicular Lymphoma (FL) **after minimal or no chemotherapy prior to histologic transformation with partial response, no response, or progressive disease after treatment**
  - Richter’s transformation of CLL to DLBCL if **ANY ONE** of the following:
    - Received two or more prior lines of systemic therapy
    - Used for treatment of disease that is in second or greater relapse
  - AIDS-related diffuse large B-cell lymphoma, **Primary Effusion Lymphoma**, DLBCL, Primary Mediastinal large B-cell lymphoma (PMBCL), high grade B-cell Lymphoma, HHV8-positive diffuse large B-cell Lymphoma not otherwise specified (NOS) **OR** Monomorphic Post-Transplant Lymphoproliferative Disorder (**PTLD**) (B-cell type) used as **ANY ONE** of the following:
    - Additional therapy for individuals with intent to proceed to transplant with partial response following second-line therapy for relapsed or refractory disease
    - Treatment of disease that is in second or greater relapse

### RENEWAL CRITERIA

- Axicabtagene ciloleucel is **NOT** considered **medically appropriate** for renewal.

INDICATION(S)	DOSAGE & ADMINISTRATION
Large B-Cell Lymphoma	<p><b>Lymphodepleting chemotherapy:</b></p> <ul style="list-style-type: none"> <li>• Administer cyclophosphamide 500 mg/m<sup>2</sup> and fludarabine 30 mg/m<sup>2</sup> intravenously on the fifth, fourth, and third day before infusion of axicabtagene ciloleucel</li> </ul> <p><b>Axicabtagene Ciloleucel Infusion:</b></p> <ul style="list-style-type: none"> <li>• Premedicate with 650 mg acetaminophen and 12.5 mg diphenhydramine 1 hour prior to infusion. Avoid prophylactic system corticosteroids which may interfere with axicabtagene ciloleucel activity.</li> <li>• Infuse the entire contents of the axicabtagene ciloleucel bag within 30 minutes by either gravity or a peristaltic pump</li> <li>• Each single infusion bag of axicabtagene ciloleucel contains a suspension of chimeric antigen receptor (CAR)-positive T cells in approximately 68 ml. The target dose is 2 × 10<sup>6</sup> CAR-positive viable T cells per kg body weight, with a maximum of 2 × 10<sup>8</sup> CAR-positive viable T cells.</li> </ul> <p><b>Monitoring:</b></p> <ul style="list-style-type: none"> <li>• Monitor patients at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of CRS and neurologic toxicities.</li> <li>• Instruct patients to remain within proximity of the certified healthcare facility for at least 4 weeks following infusion.</li> </ul>
<p>For autologous use only. For intravenous use only.</p> <ul style="list-style-type: none"> <li>• Axicabtagene ciloleucel is prepared from the patient’s peripheral blood mononuclear cells, which are obtained via a standard leukapheresis procedure</li> <li>• One treatment course consists of lymphodepleting chemotherapy followed by a single infusion of axicabtagene ciloleucel.</li> </ul>	



- Confirm axicabtagene ciloleucel availability prior to starting the lymphodepleting regimen.
- Store infusion bag in the vapor phase of liquid nitrogen (less than or equal to minus 150°C). Thaw prior to infusion.
- In case of manufacturing failure, a second manufacturing may be attempted.
- Additional chemotherapy (not the lymphodepletion) may be necessary while the patient awaits the product.
- Ensure that 2 doses of tocilizumab and emergency equipment are available prior to infusion and during the recovery period.
- Axicabtagene ciloleucel contains human blood cells that are genetically modified with replication incompetent retroviral vector. Follow universal precautions and local biosafety guidelines for handling and disposal.

## LENGTH OF AUTHORIZATION

Coverage will be provided for one treatment course (1 dose of axicabtagene ciloleucel) and may not be renewed.

Refer to **DOSAGE LIMITS** below

## APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

## IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

## ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

## SOURCES

MICROMEDEX Healthcare Series. Drugdex Evaluations. (2020, August). *Axicabtagene ciloleucel*. Retrieved November 30, 2020 from MICROMEDEX Healthcare Series.

National Comprehensive Cancer Network. (2020). NCCN Drugs & Biologics Compendium®. *Axicabtagene ciloleucel*. Retrieved November 30, 2020 from the National Comprehensive Cancer Network.

U. S. Food and Drug Administration. (2020, May). Center for Vaccines, Blood and Biologics. YESCARTA® (*axicabtagene ciloleucel*). Retrieved November 30, 2020 from <https://www.fda.gov/media/108377/download>.



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***Policy***

Medical Policy Manual

**Approved Revision: Do Not Implement Until 4/2/21**

EFFECTIVE DATE 4/2/21

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