MEDICAL MUTUAL®

Drug Policy

Policy:	**201733**	**Initial Effective Date: 10/20/2017**
Code(s):	**HCPCS Code Q2041** **NDC Codes: 71287-0119-01; 71287-0119-02** **Related CPT Codes*:** **0537T; 0538T; 0539T; 0540T**	**Annual Review Date: 01/22/2019** **Last Revised Date: 01/22/2019**
SUBJECT:	**Yescarta ® (axicabtagene ciloleucel) suspension for IV infusion**	

*CPT Codes related to Chimeric antigen receptor T-cell (CAR-T) therapy are only approvable if Car-T agent, Yescarta, has been prior approved. If there is no prior approval for Yescarta, the related CPT codes listed above will deny as investigational (M9E).

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

OVERVIEW

Yescarta (axicabtagene ciloleucel) is a CD19-directed genetically-modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. [1] Yescarta is a type of treatment called chimeric antigen receptor T cell (CAR-T) therapy, which uses the patient's own genetically altered T cells to attack cancer cells. It is the second FDA-approved CAR-T cell therapy. FDA approval is supported by data from the ZUMA-1 pivotal trial.[2]

The process of producing Yescarta begins with collecting peripheral blood mononuclear cells from the patient via apheresis. These cells are then sent to a laboratory or a pharmaceutical manufacturing facility where they are genetically engineered to produce CARs on their surface. These reengineered T cells, known as CAR-T cells, are able to recognize an antigen on targeted tumor cells. The CAR-T cells are next stimulated to multiple. The expanded population of CAR-T cells is then prepared for return to a treatment facility where they will be intravenously infused back into the patient. Time from apheresis to infusion is variable; the manufacturer aims to eventually reach a 16-18-day "vein-to-vein" duration. Patients will receive a conditioning chemotherapy regimen to deplete T lymphocytes prior to their Yescarta infusion.[3]

Yescarta has black boxed warnings for cytokine release syndrome (CRS) and neurological toxicities. Because of the risk of CRS and neurological toxicities, Yescarta is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called Yescarta REMS. Healthcare facilities that dispense and administer Yescarta must be enrolled and comply with the REMS requirements. Certified healthcare facilities must have on-site, immediate access to tocilizumab, and ensure that a minimum of two doses of tocilizumab are available for each patient for administration within 2 hours after Yescarta infusion, if needed for treatment of CRS. Certified healthcare facilities must ensure that

healthcare providers who prescribe, dispense or administer Yescarta are trained about the management of CRS and neurological toxicities.[1]

POLICY STATEMENT

This policy involves the use of Yescarta. Prior authorization is recommended for medical and pharmacy benefit coverage of Yescarta. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. The requirement that the patient meet the Criteria for coverage of the requested medication applies to the initial authorization only. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria.Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Yescarta as well as the monitoring required for AEs and long-term efficacy, initial approval requires Yescarta be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Yescarta is recommended in those who meet the following criteria:

Food and Drug Administration (FDA)-Approved Indications

Non-Hodgkin Lymphoma (NHL): Large B-cell lymphoma, relapsed or refractory

Criteria. *Patient must meet the following criteria (A, B, C, D, E, F, G, H. I, J, K, L, M, N, O, P, and Q):*
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A) Patient is 18 years of age or older and is not pregnant; AND
B) Patient must have CD 19 Tumor expression in bone marrow or peripheral blood [documentation required]; AND
C) Patient has been diagnosed with NHL Large B-cell lymphoma AND patient meets ONE Of the following criteria (i, ii, iii or iv)
    i. Patient has diffuse large B-cell Lymphoma (DLBCL) not otherwise specified; OR
    ii. Patient has primary mediastinal large B-cell lymphoma; OR
    iii. Patient has high grade B-cell lymphoma; OR
    iv. Patient has DLBCL arising from follicular lymphoma; AND
D) Patient meets ONE of the following criteria (i, ii, iii or iv):
    i. Patient had relapse following second or subsequent complete remissions (post-chemotherapy); OR
    ii. Patient is chemotherapy-refractory to second-line or later lines of therapy; OR
    iii. Patient has received prior chemotherapy for follicular lymphoma and subsequently have chemorefractory disease and received 2 or more lines of chemotherapy after transformation to DLBCL; OR
    iv. Patient has had prior autologous stem cell transplantation (ASCT) that has progressed within a year post stem cell infusion; AND
E) Previous therapy included anthracycline chemotherapy agent and an anti-CD 20 antibody; AND

F) Patient has not previously been treated with a CAR-T therapy or Yescarta; AND
G) Patient does not have history or presence of CNS disorder such as seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, or any autoimmune disease with CNS involvement; AND
H) Yescarta is prescribed by and administered by an oncologist who are trained about the management of CRS and neurological toxicities; AND
I) Asymptomatic or minimally symptomatic with Eastern Cooperative Oncology Group (ECOG) performance status 0-1†; AND
J) Patient does not have history of allogeneic stem cell transplantation; AND
K) Patient will receive Yescarta from a certified healthcare facility that is enrolled and complies with Yescarta REMS requirements; AND
L) Patient will be treated with one treatment course of fludarabine and cyclophosphamide lymphodepleting chemotherapy prior to infusion of Yescarta- fludarabine (30 mg/m^2 intravenously daily) and cyclophosphamide (500 mg/m^2 intravenously daily) on the fifth, fourth and third day before infusion; AND
M) Yescarta infusion will be delayed if a patient has unresolved serious adverse reactions (including pulmonary reactions, cardiac reactions, or hypotension) from preceding chemotherapies, active uncontrolled infection, active graft vs host disease (GVHD), or worsening of leukemia burden following lymphodepleting chemotherapy; AND
N) Patient will be monitored for signs and symptoms of CRS for at least daily for 7 days after treatment with Yescarta and will be counselled to seek immediate medical attention should signs or symptoms of CRS or a neurological event occur at any time; AND
O) Patient will not receive a G-CSF agent within the first 3 weeks after Yescarta infusion or until CRS has resolved; AND
P) Patient will not receive a live virus vaccine for at least 6 weeks prior to the start of lymphodepleting chemotherapy, during Yescarta treatment and until immune recovery following treatment with Yescarta; AND
Q) Patient will stay within proximity of the Yescarta infusion center for at least 4 weeks following infusion.

Dosing in NHL Large B-cell lymphoma:
Dosing of Yescarta is based on the number of chimeric antigen receptor (CAR)-positive viable T cells.

The target Yescarta dose is:

2 × 106 CAR-positive viable T cells per kg body weight, with a maximum of 2 × 108 CAR-positive viable T cells.[1]

Initial Approval/ Extended Approval.
A) *Initial Approval: Approve for 90 days for 1 single-dose of Yescarta per lifetime*
B) *Extended Approval: not recommended*

Duration of Therapy in NHL Large B-cell lymphoma: 1 single-dose of Yescarta.

Labs/Diagnostics. Perform screening for HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing of Yescarta. Monitor immunoglobulin levels after treatment with Yescarta and manage using infection precautions, antibiotic prophylaxis and immunoglobulin replacement standard guidelines.[1]

†Eastern Cooperative Oncology Group Performance Status:

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

CONDITIONS NOT RECOMMENDED FOR APPROVAL

1. **Active infection or inflammatory disorders.** Do not administer Yescarta to patients with active infection or inflammatory disorders (including TB, HBV, HCV, and HIV).[1]
2. **Primary central nervous system lymphoma**. Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma, detectable cerebrospinal fluid malignant cells, or brain metastases, or with a history of CNS lymphoma, cerebrospinal fluid malignant cells or brain metastases
3. **Richters Syndrome (or Richters Transformation).** Yescarta is not indicated for the treatment of patients with DLBCL that transformed from CLL with Richters Syndrome or Richters Transformation.
4. **Other Cancer Indications**. Coverage is not recommended for circumstances not listed in the Authorization Criteria (FDA-approved indications). Criteria will be updated as new published data are available. [1]

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Yescarta (axicabtagene ciloleucel) [prescribing information]. Santa Monica, CA: Kite Pharma, Inc.; October 2017.
2. Phase 1 Results of ZUMA-1: A Multicenter Study of KTE-C19 Anti-CD19 CAR T Cell Therapy in Refractory Aggressive Lymphoma. Locke, Frederick L. et al. Molecular Therapy , Volume 25 , Issue 1 , 285 – 295.

3. Yescarta (axicabtagene ciloleucel). Hayes. Transforming Healthcare with Evidence https://www.hayesinc.com/subscribers/displaySubscriberArticle.do?articleUid=pg.axicabtagene
4. The Leukemia & Lymphoma Society (LLS). Ph-Positive ALL Therapy. Available at https://www.lls.org/leukemia/acute-lymphoblastic-leukemia/treatment/ph-positive-all-therapy
5. Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. N Engl J Med. 2017;377(26):2531-2544.
6. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 3.2018 – April 13, 2018). © 2018 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed January 21, 2019.

FOR MEDICAL BENEFIT COVERAGE REQUESTS:

Prior approval is required for HCPCS Codes Q2041

HCPCS Code(s):	
Q2041	Axicabtagene Ciloleucel, up to 200 million autologous Anti-CD19 CAR T Cells, Including leukapheresis and dose preparation procedures, per infusion (effective date 4/1/2018)