MetroPlus Health

Policy and Procedure

Title: Yescarta (axicabtagene ciloleucel)	**Division: Medical Management** **Department: Utilization Management**
Approval Date: 3/30/2018	**LOB: Medicaid, HIV SNP, HARP, CHP, MetroPlus Gold, GoldCare, Marketplace, Essential, Medicare, Ultracare**
Effective Date: 3/30/2018	**Policy Number: UM-MP230**
Review Date: 1/28/2025	**Cross Reference Number:**
Retired Date:	**Page 1 of 12**

I. POLICY DESCRIPTION

Immunological Agent, Yescarta (Rx)

II. RESPONSIBLE PARTIES

Medical Management Administration, Utilization Management, Integrated Care Management, Pharmacy, Claims Department, Provider Contracting.

III. DEFINITIONS

Yescarta (Axicabtagene ciloleucel) is a CD19-directed genetically modified autologous T-cell immunotherapy which binds to CD19-expressing cancer cells and normal B cells. As studies have shown, 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. This results in secretion of inflammatory cytokines and chemokines which relays messages that coordinate the immune system to fend off attackers. As a result, this sequence of events leads to killing of CD19-expressing cells.

Yescarta is indicated for the treatment of:

Adult patients with large B-cell lymphoma that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy.

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.

Adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy. This indication is approved under accelerated approval based on response rate.

IV. POLICY

For Medicare and Ultracare Only: Per CMS regulation, Metroplus Health Plan follows the following National Coverage Determination (NCD) for Chimeric Antigen Receptor (CAR) T-cell Therapy

1. NCD 110.24

For all non-Medicare LOBs:
Yescarta will be considered medically necessary once the following coverage criteria is met. Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

INITIAL REQUEST:

1. Adult Large B-cell lymphoma

A. Member is 18 years of age or older;

AND

B. Member has a diagnosis confirmed by submitted documentation including chart notes consistent with ONE of the following:

- **a.** Large B-cell lymphoma;

  OR

- **b.** Diffuse large B-cell lymphoma (DLBCL) not otherwise specified;

  OR

- **c.** Primary mediastinal large B-cell lymphoma;

  OR

- **d.** High grade B-cell lymphoma;

  OR

- **e.** DLBCL arising from follicular lymphoma;

AND

C. ONE of the following:

- **a.** Member has disease refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy
  (Examples of chemoimmunotherapy include:
  RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone);
  Pola-R-CHP (polatuzumab vedotin-piiq, rituximab, cyclophosphamide, doxorubicin, prednisone));

  OR

- **b.** Member has relapsed or refractory disease after two or more lines of systemic therapy
  (*Examples of systemic therapy include:*
  CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Gazyva (obinutuzumab intravenous infusion) or rituximab products;

CVP (cyclophosphamide, vincristine, prednisone) + rituximab products; lenalidomide + rituximab products));

AND

D. Member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1;

AND

E. Member does not have ANY of the following *(Note: If member has any of the following then attestation needs to be provided which states that member is being followed by a neurologist, infection disease speciliast or any other qualified physician per condition to monitor member if Yescarta is still to be given per physician's discretion)*:

a. History of malignancy other than nonmelanoma skin cancer or carcinoma in situ (e.g. cervix, bladder, breast) or follicular lymphoma unless disease free for at least 3 years;

OR

b. History or presence of clinically relevant central nervous system (CNS) pathology **(**e.g., seizure disorders, paresis, aphasia, stroke, severe brain injuries, organic brain syndrome, cerebellar disease, dementia, Parkinson's disease, and or psychosis);

OR

c. Active uncontrolled infection including human immunodeficiency virus (HIV), Hepatitis B or C and Cytomegalovirus (CMV), systemic fungal, bacterial, viral, or other infection that is not controlled;

AND

F. Member will not receive live vaccines 6 weeks prior to the start of lymphodepleting chemotherapy, during Yescarta treatment, and until immune recovery following treatment with Yescarta;

AND

G. Member has adequate organ function as defned by ALL of the following *(Note: If member does not meet any of the following then attestation needs to be provided which states that member is being followed by a qualified physician per condition to monitor member if Yescarta is still to be given per physician's discretion)*:

a. Member has a creatinine clearance ≥ 60 mL/min;

AND

b. Alanine aminotransferase ≤ 2.5 times the upper limit of normal;

AND

c. Left ventricular ejection fraction (LVEF) ≥ 50%;

AND

H. Member has adequate bone marrow function to receive lymphodepleting chemotherapy as determined by the prescriber;

AND

I. Member is not currently enrolled in Large B-cell lymphoma clinical trial or is ineligible for clinical trial enrollment;

AND

J. Member has not previously been treated with Yescarta or any other CAR-T therapy;

AND

K. The requesting provider belongs to a healthcare facility that has enrolled in the Yescarta REMS (Risk Evaluation and Mitigation Strategy) program and training has been given to providers on the management of cytokine release syndrome (CRS) and neurological toxicities (treatment centers can be found here);

AND

L. Authorization is for no more than one dose

2. Adult Follicular lymphoma

A. Member is 18 years of age or older;

AND

B. Member has a diagnosis of Follicular lymphoma confirmed by submitted documentation including chart notes;

AND

C. Member has relapsed or refractory disease after trial and failure or contraindication to at least TWO lines of therapy that includes a combination of an anti-CD 20 monoclonal antibody (e.g., Rituxan (rituximab), Gazyva (Obinutuzumab)) and an alkylating agent (e.g., bendamustine, cyclophosphamide, chlorambucil);
(Examples of systemic therapy include:
Bendamustine + obinutuzumab or rituximab;
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + binutuzumab or rituximab;
CVP (cyclophosphamide, vincristine, prednisone) + obinutuzumab or rituximab;
Lenalidomide + rituximab;
Chlorambucil ± rituximab;
Cyclophosphamide ± rituximab))

AND

D. Member has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1;

AND

E. Member does not have ANY of the following *(Note: If member has any of the following then attestation needs to be provided which states that member is being followed by a neurologist, infection disease speciliast or any other qualified physician per condition to monitor member if Yescarta is still to be given per physician's discretion)*:

- **a.** History of malignancy other than nonmelanoma skin cancer or carcinoma in situ (e.g. cervix, bladder, breast) or follicular lymphoma unless disease free for at least 3 years;

OR

- **b.** History or presence of clinically relevant central nervous system (CNS) pathology (e.g., seizure disorders, paresis, aphasia, stroke, severe brain injuries, organic brain syndrome, cerebellar disease, dementia, Parkinson's disease, and or psychosis);

OR

- **c.** Active uncontrolled infection including human immunodeficiency virus (HIV), Hepatitis B or C and Cytomegalovirus (CMV), systemic fungal, bacterial, viral, or other infection that is not controlled;

AND

F. Member will not receive live vaccines 6 weeks prior to the start of lymphodepleting chemotherapy, during Yescarta treatment, and until immune recovery following treatment with Yescarta;

AND

G. Member has adequate organ function as defned by ALL of the following *(Note: If member does not meet any of the following then attestation needs to be provided which states that member is being followed by a qualified physician per condition to monitor member if Yescarta is still to be given per physician's discretion)*:

- **a.** Member has a creatinine clearance ≥ 60 mL/min;

AND

- **b.** Alanine aminotransferase ≤ 2.5 times the upper limit of normal;

AND

- **c.** Left ventricular ejection fraction (LVEF) ≥ 50%;

AND

H. Member has adequate bone marrow function to receive lymphodepleting chemotherapy as determined by the prescriber;

AND

I. Member is not currently enrolled in Follicular lymphoma clinical trial or is ineligible for clinical trial enrollment;

AND

J. Member has not previously been treated with Yescarta or any other CAR-T therapy; **AND**

K. The requesting provider belongs to a healthcare facility that has enrolled in the Yescarta REMS (Risk Evaluation and Mitigation Strategy) program and training has been given to providers on the management of cytokine release syndrome (CRS) and neurological toxicities (treatment centers can be found here);

Initial Duration of Approval: *One single dose per lifetime*

RENEWAL REQUEST:

Repeat administration of Yescarta is investigational and will not be covered.

Renewal Duration of Approval: *Not Applicable*

3. LIMITATIONS/EXCLUSIONS:

A. Repeat administration of Yescarta is considered experimental and investigational because there have been no established studies to demonstrate effectiveness

B. Yescarta is also considered experimental or investigational for the following indications due to no established studies of clinical efficacy:

- **a.** Acute lymphoblastic leukemia (ALL)
- **b.** Indolent non-Hodgkin lymphoma (NHL)
- **c.** Mantle cell lymphoma
- **d.** Marginal zone lymphoma
- **e.** Primary central nervous system (CNS) lymphoma

C. Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma

4. APPLICABLE PROCEDURE CODES

CPT Code	Description
Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 CAR T cells, including leukopheresis and dose preparation procedures, per infusion

5. APPLICABLE DIAGNOSIS CODES:

CODE	Description
C82.00	Follicular lymphoma grade I, unspecified site
C82.01	Follicular lymphoma grade I, lymph nodes of head, face, and neck
C82.02	Follicular lymphoma grade I, intrathoracic lymph nodes

C82.03	Follicular lymphoma grade I, intra-abdominal lymph nodes
C82.04	Follicular lymphoma grade I, lymph nodes of axilla and upper limb
C82.05	Follicular lymphoma grade I, lymph nodes of inguinal region and lower limb
C82.06	Follicular lymphoma grade I, intrapelvic lymph nodes
C82.07	Follicular lymphoma grade I, spleen
C82.08	Follicular lymphoma grade I, lymph nodes of multiple sites
C82.09	Follicular lymphoma grade I, extranodal and solid organ sites
C82.10	Follicular lymphoma grade II, unspecified site
C82.11	Follicular lymphoma grade II, lymph nodes of head, face, and neck
C82.12	Follicular lymphoma grade II, intrathoracic lymph nodes
C82.13	Follicular lymphoma grade II, intra-abdominal lymph nodes
C82.14	Follicular lymphoma grade II, lymph nodes of axilla and upper limb
C82.15	Follicular lymphoma grade II, lymph nodes of inguinal region and lower limb
C82.16	Follicular lymphoma grade II, intrapelvic lymph nodes
C82.17	Follicular lymphoma grade II, spleen
C82.18	Follicular lymphoma grade II, lymph nodes of multiple sites
C82.19	Follicular lymphoma grade II, extranodal and solid organ sites
C82.20	Follicular lymphoma grade III, unspecified, unspecified site
C82.21	Follicular lymphoma grade III, unspecified, lymph nodes of head, face, and neck
C82.22	Follicular lymphoma grade III, unspecified, intrathoracic lymph nodes
C82.23	Follicular lymphoma grade III, unspecified, intra-abdominal lymph nodes
C82.24	Follicular lymphoma grade III, unspecified, lymph nodes of axilla and upper limb
C82.25	Follicular lymphoma grade III, unspecified, lymph nodes of inguinal region and lower limb
C82.26	Follicular lymphoma grade III, unspecified, intrapelvic lymph nodes
C82.27	Follicular lymphoma grade III, unspecified, spleen
C82.28	Follicular lymphoma grade III, unspecified, lymph nodes of multiple sites
C82.29	Follicular lymphoma grade III, unspecified, extranodal and solid organ sites
C82.30	Follicular lymphoma grade IIIa, unspecified site
C82.31	Follicular lymphoma grade IIIa, lymph nodes of head, face, and neck
C82.32	Follicular lymphoma grade IIIa, intrathoracic lymph nodes
C82.33	Follicular lymphoma grade IIIa, intra-abdominal lymph nodes
C82.34	Follicular lymphoma grade IIIa, lymph nodes of axilla and upper limb
C82.35	Follicular lymphoma grade IIIa, lymph nodes of inguinal region and lower limb
C82.36	Follicular lymphoma grade IIIa, intrapelvic lymph nodes
C82.37	Follicular lymphoma grade IIIa, spleen

C82.38	Follicular lymphoma grade IIIa, lymph nodes of multiple sites
C82.39	Follicular lymphoma grade IIIa, extranodal and solid organ sites
C82.40	Follicular lymphoma grade IIIb, unspecified site
C82.41	Follicular lymphoma grade IIIb, lymph nodes of head, face, and neck
C82.42	Follicular lymphoma grade IIIb, intrathoracic lymph nodes
C82.43	Follicular lymphoma grade IIIb, intra-abdominal lymph nodes
C82.44	Follicular lymphoma grade IIIb, lymph nodes of axilla and upper limb
C82.45	Follicular lymphoma grade IIIb, lymph nodes of inguinal region and lower limb
C82.46	Follicular lymphoma grade IIIb, intrapelvic lymph nodes
C82.47	Follicular lymphoma grade IIIb, spleen
C82.48	Follicular lymphoma grade IIIb, lymph nodes of multiple sites
C82.49	Follicular lymphoma grade IIIb, extranodal and solid organ sites
C82.50	Diffuse follicle center lymphoma, unspecified site
C82.51	Diffuse follicle center lymphoma, lymph nodes of head, face, and neck
C82.52	Diffuse follicle center lymphoma, intrathoracic lymph nodes
C82.53	Diffuse follicle center lymphoma, intra-abdominal lymph nodes
C82.54	Diffuse follicle center lymphoma, lymph nodes of axilla and upper limb
C82.55	Diffuse follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.56	Diffuse follicle center lymphoma, intrapelvic lymph nodes
C82.57	Diffuse follicle center lymphoma, spleen
C82.58	Diffuse follicle center lymphoma, lymph nodes of multiple sites
C82.59	Diffuse follicle center lymphoma, extranodal and solid organ sites
C82.60	Cutaneous follicle center lymphoma, unspecified site
C82.61	Cutaneous follicle center lymphoma, lymph nodes of head, face, and neck
C82.62	Cutaneous follicle center lymphoma, intrathoracic lymph nodes
C82.63	Cutaneous follicle center lymphoma, intra-abdominal lymph nodes
C82.64	Cutaneous follicle center lymphoma, lymph nodes of axilla and upper limb
C82.65	Cutaneous follicle center lymphoma, lymph nodes of inguinal region and lower limb
C82.66	Cutaneous follicle center lymphoma, intrapelvic lymph nodes
C82.67	Cutaneous follicle center lymphoma, spleen
C82.68	Cutaneous follicle center lymphoma, lymph nodes of multiple sites
C82.69	Cutaneous follicle center lymphoma, extranodal and solid organ sites
C82.80	Other types of follicular lymphoma, unspecified site
C82.81	Other types of follicular lymphoma, lymph nodes of head, face, and neck
C82.82	Other types of follicular lymphoma, intrathoracic lymph nodes

C82.83	Other types of follicular lymphoma, intra-abdominal lymph nodes
C82.84	Other types of follicular lymphoma, lymph nodes of axilla and upper limb
C82.85	Other types of follicular lymphoma, lymph nodes of inguinal region and lower limb
C82.86	Other types of follicular lymphoma, intrapelvic lymph nodes
C82.87	Other types of follicular lymphoma, spleen
C82.88	Other types of follicular lymphoma, lymph nodes of multiple sites
C82.89	Other types of follicular lymphoma, extranodal and solid organ sites
C82.90	Follicular lymphoma, unspecified, unspecified site
C82.91	Follicular lymphoma, unspecified, lymph nodes of head, face, and neck
C82.92	Follicular lymphoma, unspecified, intrathoracic lymph nodes
C82.93	Follicular lymphoma, unspecified, intra-abdominal lymph nodes
C82.94	Follicular lymphoma, unspecified, lymph nodes of axilla and upper limb
C82.95	Follicular lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C82.96	Follicular lymphoma, unspecified, intrapelvic lymph nodes
C82.97	Follicular lymphoma, unspecified, spleen
C82.98	Follicular lymphoma, unspecified, lymph nodes of multiple sites
C82.99	Follicular lymphoma, unspecified, extranodal and solid organ sites
C83.30	Diffuse large B-cell lymphoma, unspecified site
C83.31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.32	Diffuse large B-cell lymphoma, intrathoracic lymph nodes
C83.33	Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
C83.34	Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
C83.35	Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.36	Diffuse large B-cell lymphoma, intrapelvic lymph nodes
C83.37	Diffuse large B-cell lymphoma, spleen
C83.38	Diffuse large B-cell lymphoma, lymph nodes of multiple sites
C83.39	Diffuse large B-cell lymphoma, extranodal and solid organ sites
C85.10	Unspecified B-cell lymphoma, unspecified site
C85.11	Unspecified B-cell lymphoma, lymph nodes of head, face, and neck
C85.12	Unspecified B-cell lymphoma, intrathoracic lymph nodes
C85.13	Unspecified B-cell lymphoma, intra-abdominal lymph nodes
C85.14	Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb
C85.15	Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.16	Unspecified B-cell lymphoma, intrapelvic lymph nodes
C85.17	Unspecified B-cell lymphoma, spleen

C85.18	Unspecified B-cell lymphoma, lymph nodes of multiple sites
C85.19	Unspecified B-cell lymphoma, extranodal and solid organ sites
C85.20	Mediastinal (thymic) large B-cell lymphoma, unspecified site
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites

6. REFERENCES

1. Food and Drug Administration. FDA approves CAR-T cell therapy to treat adults with certain types of large B-cell lymphoma. FDA: Silver Spring, MD. October 18, 2017. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-car-t-cell-therapy-treat-adults-certain-types-large-b-cell-lymphoma
2. Highlights of Prescribing Information. Yescarta (axicabtagene ciloleucel) suspension for intravenous infusion. Initial U.S. Approval: October 2017. Kite Pharma, Inc. Santa Monica, CA. Available at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/yescarta/yescarta-pi.pdf
3. IBM Micromedex. Available at: micromedexsolutions.com
4. Kite Pharma, Inc. A Phase 1-2 multi-center study evaluating KTE-C19 in subjects with refractory aggressive non-hodgkin lymphoma (ZUMA-1). NCT 02348216. Updated December 14, 2017. Available at: https://clinicaltrials.gov/ct2/show/NCT02348216?term=zuma+kte&rank=2.

5. The NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 1.2024; January 18, 2024).© 2021 National Comprehensive Cancer Network, Inc. https://www.nccn.org
6. Yescarta [Product Information], Kite Pharma, Santa Monica, California; June 2024. Available at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/yescarta/yescarta-pi.pdf
7. The NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 1.2024; January 18, 2024).© 2021 National Comprehensive Cancer Network, Inc. https://www.nccn.org.
8. NCD - Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24). www.cms.gov. Available at: NCD - Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24) (cms.gov)
9. Study Evaluating the Safety and Efficacy of KTE-C19 in Adult Participants With Refractory Aggressive Non-Hodgkin Lymphoma (ZUMA-1). ClinicalTrials.gov ID: NCT02348216. Available at: https://clinicaltrials.gov/study/NCT02348216
10. Study of Effectiveness of Axicabtagene Ciloleucel Compared to Standard of Care Therapy in Patients With Relapsed/Refractory Diffuse Large B Cell Lymphoma (ZUMA-7). ClinicalTrials.giv ID: NCT03391466. Available at: https://clinicaltrials.gov/study/NCT03391466

REVISION LOG:

REVISIONS	DATE
Creation date	3/30/2018
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Annual Review	9/1/2021
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Review	4/23/2024
Updated review	1/28/2025

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Approved: **Date:** David Ackman Digitally signed by David Ackman Date: 2025.01.30 12:00:52 -05'00'	**Approved:** **Date:** Sanjiv Shah MD Digitally signed by Sanjiv Shah MD Date: 2025.01.30 16:27:56 -05'00'
David Ackman, MD **VP of Medical Director**	**Sanjiv Shah, MD** **Chief Medical Officer**

Medical Guideline Disclaimer:

 The treating physician or primary care provider must submit MetroPlus Health Plan clinical evidence that the patient meets the criteria for the treatment or surgical procedure. Without this documentation and information, MetroPlus Health Plan will not be able to properly review the request for prior authorization. The clinical review criteria expressed in this policy reflects how MetroPlus Health Plan determines whether certain services or supplies are medically necessary. MetroPlus Health Plan established the clinical review criteria based upon a review of currently available clinical information(including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). MetroPlus Health Plan expressly reserves the right to revise these conclusions as clinical information changes, and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by MetroPlus Health Plan, as some programs exclude coverage for services or supplies that MetroPlus Health Plan considers medically necessary. If there is a discrepancy between this guidelines and a member's benefits program, the benefits program will govern. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and website links are accurate at time of publication.