

Medical Policy:

YESCARTA® (axicabtagene ciloleucel)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.42	March 7, 2025	

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The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as “EmblemHealth”), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth 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). EmblemHealth 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 EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. 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 web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Yescarta (axicabtagene ciloleucel): is a CD19-directed genetically modified autologous T cell immunotherapy that kills CD19-expressing cancer cells. T cells from the patient are harvested and genetically modified ex vivo by retroviral transduction to express a chimeric antigen receptor (CAR), and after infusion back into the patient, results in CD28 and CD3-zeta co-stimulatory domains to activate causing T-cell activation, proliferation, acquisition of effector functions and secretion of inflammatory cytokines and chemokines.

Yescarta is FDA approved for:

Follicular lymphoma that has relapsed or is refractory after two or more lines of systemic therapy. This indication was approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials(s).

Large B-cell lymphoma in the following situations:

1. Disease that is refractory to first-line chemoimmunotherapy or relapses within 12 months of first-line chemoimmunotherapy.
2. Relapsed or refractory disease after two or more lines of systemic therapy, including diffuse B-cell lymphoma (DLBCL) not otherwise specified, primarily mediastinal large B-cell lymphoma, high-grade B-cell lymphoma,

and DLBCL arising from follicular lymphoma.

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

Length of Authorization

I. Initial Approval

- Approval will be granted for 1 single dose of Yescarta

II. Renewal

- Coverage cannot be renewed, a maximum of one dose per lifetime will apply

Dosing Limits [Medical Benefit]

Quantity Limit (max daily dose) [NDC Unit]:

- 1 infusion bag of up to 200 million autologous anti-CD19 CAR-positive viable T-cells

Max Units (per dose and over time) [HCPCS Unit]:

- 1 billable unit (1 infusion of up to 200 million autologous anti-CD19 CAR-positive viable T-cells)

Guideline

I. Initial Approval Criteria

Provider must submit documentation (which may include office notes and lab results) supporting that the patient has met all approval criteria.

1. Patient is at least 18 years of age, unless otherwise specified; **AND**
2. Patient does not have a clinically significant active systemic infection or inflammatory disorder; **AND**
3. Patient has not received live vaccines within 6 weeks prior to the start of lymphodepleting chemotherapy, and will not receive live vaccines during axicabtagene ciloleucel treatment and until immune recovery following treatment; **AND**
4. Patient has been screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines prior to collection of cells (leukapheresis); **AND**
5. Prophylaxis for infection will be followed according to local guidelines; **AND**
6. Healthcare facility must be enrolled in and comply with the requirements of the YESCARTA & TECARTUS REMS Program; **AND**
7. Patient has not received prior CAR-T therapy; **AND**
8. Patient has not received other anti-CD19 therapy (e.g., blinatumomab, tafasitamab, loncastuximab tesirine, etc.) OR patient previously received other anti-CD19 therapy and re-biopsy indicates CD-19 positive disease; **AND**
9. Used as a single agent (not applicable to lymphodepleting or additional chemotherapy while awaiting manufacture); **AND**
10. Patient has an ECOG performance status of 0-1; **AND**
11. Patient does not have primary central nervous system lymphoma; **AND**

A. B-Cell Lymphomas †

- i. Patient has histologic transformation of follicular lymphoma (indolent lymphoma) to diffuse large B-cell lymphoma (DLBCL); **AND**
 - a. Disease is refractory to first-line chemoimmunotherapy; **OR**
 - b. Used for treatment of disease that has relapsed within 12 months of first-line chemoimmunotherapy; **OR**

- c. Patient has received two (2) or more prior lines of chemoimmunotherapy for indolent or transformed disease which must have included an anthracycline-based regimen, unless contraindicated; **OR**
- ii. Patient has histologic transformation of marginal zone lymphoma (indolent lymphoma) to DLBCL **OR** Richter's transformation of CLL to DLBCL; **AND**
 - a. Patient has received two (2) or more prior lines of chemoimmunotherapy for indolent or transformed disease which must have included an anthracycline-based regimen, unless contraindicated; **OR**
- iii. Patient has HIV-related large B-cell lymphoma (i.e., HIV-related DLBCL, primary effusion lymphoma, or HHV8-positive DLBCL, not otherwise specified), DLBCL, primary mediastinal large B-cell lymphoma (PMBCL), high grade B-cell lymphoma, or monomorphic post-transplant lymphoproliferative disorder (B-cell type); **AND**
 - a. Used as additional therapy for relapsed disease >12 months after completion of first-line therapy and partial response following second-line therapy; **OR**
 - b. Used as additional therapy for patients with primary refractory disease (partial response, no response, or progression) or relapsed disease <12 months after completion of first-line therapy; **OR**
 - c. Used for treatment of disease that is in second or greater relapse in patients with partial response, relapse, or progressive disease following therapy for relapsed or refractory disease; **OR**
- iv. Patient has nodal marginal zone lymphoma (MZL) or follicular lymphoma (grade 1, 2 or 3A); **AND**
 - a. Used as third-line and subsequent therapy for partial response, no response, relapsed, or progressive disease; **OR**
- v. Patient has extranodal marginal zone lymphoma (EMZL) of the stomach or of nongastric sites (noncutaneous); **AND**
 - a. Used as third-line and subsequent therapy for relapsed, refractory, or progressive disease; **OR**
- vi. Patient has splenic marginal zone lymphoma (MZL); **AND**
 - a. Used as third-line and subsequent therapy for disease recurrence **AND**
- vii. Patient will be using Yescarta (axicabtagene ciloleucel) at a treatment center that is certified to administer Yescarta (axicabtagene ciloleucel); **AND**
- viii. Patient will be monitored for signs and symptoms of Cytokine Release Syndrome (CRS) for at least 4 weeks after treatment with Yescarta (axicabtagene ciloleucel) and will be counselled to seek immediate medical attention should signs and symptoms of CRS or a neurological event occur at any time; **AND**
- ix. Patient will stay within proximity (within 2 hours) of the Yescarta (axicabtagene ciloleucel) infusion center for at least 4 weeks following infusion.

Dosing/Administration

Yescarta (axicabtagene ciloleucel) is available as cell suspension for infusion. Yescarta comprises a suspension of 2×10^6 CAR-positive viable T cells per kg of body weight, with a maximum of 2×10^8 CAR-positive viable T cells in approximately 68 mL.

1. Dosing of Yescarta (axicabtagene ciloleucel) is based on the number of chimeric antigen receptor (CAR)-positive viable T-cells.
2. The target dose is: 2×10^6 CAR-positive viable T cells per kg body weight, with a maximum of 2×10^8 CAR-positive viable T cells.

Applicable Procedure Codes

Code	Description
Q2041	Axicabtagene Ciloleucel, up to 200 million autologous Anti-CD19 CAR T Cells, including leukapheresis and dose preparation procedures, per infusion

Applicable NDCs

Code	Description
71287-0119-02	Yescarta Plastic Bag, Injection
71287-0119-01	Yescarta Plastic Bag, Injection

ICD-10 Diagnoses

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 regional 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
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
C83.398	Diffuse large B-cell lymphoma of other extranodal and solid organ sites
C83.80	Other non-follicular lymphoma, unspecified site
C83.81	Other non-follicular lymphoma, lymph nodes of head, face and neck
C83.82	Other non-follicular lymphoma, intrathoracic lymph nodes
C83.83	Other non-follicular lymphoma, intra-abdominal lymph nodes
C83.84	Other non-follicular lymphoma, lymph nodes of axilla and upper limb
C83.85	Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb
C83.86	Other non-follicular lymphoma, intrapelvic lymph nodes
C83.87	Other non-follicular lymphoma, spleen
C83.88	Other non-follicular lymphoma, lymph nodes of multiple sites
C83.89	Other non-follicular lymphoma, extranodal and solid organ sites
C83.90	Non-follicular (diffuse) lymphoma, unspecified site
C83.91	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of head, face, and neck
C83.92	Non-follicular (diffuse) lymphoma, unspecified intrathoracic lymph nodes
C83.93	Non-follicular (diffuse) lymphoma, unspecified intra-abdominal lymph nodes
C83.94	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of axilla and upper limb
C83.95	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of inguinal region and lower limb
C83.96	Non-follicular (diffuse) lymphoma, unspecified intrapelvic lymph nodes
C83.97	Non-follicular (diffuse) lymphoma, unspecified spleen
C83.98	Non-follicular (diffuse) lymphoma, unspecified lymph nodes of multiple sites
C83.99	Non-follicular (diffuse) lymphoma, unspecified 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
C85.80	Other specified types of non-Hodgkin lymphoma, unspecified site
C85.81	Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face and neck
C85.82	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
C85.83	Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes
C85.84	Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb
C85.85	Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region of lower limb
C85.86	Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes
C85.87	Other specified types of non-Hodgkin lymphoma, spleen
C85.88	Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma]
C88.40	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-lymphoma] not having achieved remission
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	3/7/2025	<p>Addition of Patient has an ECOG performance status of 0-1; AND • Patient does not have primary central nervous system lymphoma.</p> <p>Addition of Dosing Limits [Medical Benefit]</p> <p>Quantity Limit (max daily dose) [NDC Unit]: •1 infusion bag of up to 200 million autologous anti-CD19 CAR-positive viable T-cells Max Units (per dose and over time) [HCPCS Unit]:•1 billable unit (1 infusion of up to 200 million autologous anti-CD19 CAR-positive viable T-cells)</p> <p>Separated initial approval criteria and individual diagnosis requirements</p>
EmblemHealth & ConnectiCare	1/2/2024	<p>Annual Review:</p> <p><u>Initial Criteria:</u></p> <p>Replaced “Acquired immune deficiency syndrome (AIDS)” with “Human immunodeficiency virus (HIV)” -related B-cell lymphoma; OR</p> <p>Added “Primary effusion lymphoma; OR”</p> <p>Removed: “Patient’s disease is relapsed, or refractory defined as one of the following:</p> <ol style="list-style-type: none"> a. Relapse within 1 year after autologous hematopoietic stem cell transplantation (HSCT); OR <p>Refractory disease to the most recent therapy; AND “</p>
EmblemHealth & ConnectiCare	3/6/2023	Annual Review: No Revisions
EmblemHealth & ConnectiCare	10/27/2022	<ol style="list-style-type: none"> 1. Added Follicular lymphoma indication 2. Added Gastric MALT lymphoma; Nongastric MALT lymphoma (noncutaneous); Nodal marginal zone lymphoma; Splenic marginal zone lymphoma 3. Removal of Patient has an ECOG performance status of 0-1; AND Patient has CD19-positive disease; 4. Removed patient will be using Yescarta in conjunction with lymphodepleting chemotherapy (fludarabine 30 mg/m2 daily for 3 days and cyclophosphamide 500

		mg/m2 daily on the fifth, fourth, and third day before infusion of Yescarta
EmblemHealth & ConnectiCare	12/30/2020	Annual review

References

1. Yescarta [package insert]. Santa Monica, CA; Kite Pharma, Inc., October 2024.
2. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2024.