Medical Policy:

YESCARTA® (axicabtagene ciloleucel)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.42	January 2, 2024	

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

Guideline

I. Initial

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

Yescarta is considered medically necessary when all the below criteria are met:

1. Patient is aged 18 years or greater; **AND**
2. Patient has a confirmed diagnosis of **ONE** of the following:
    a. Follicular lymphoma; **OR**
    b. Diffuse large B-cell lymphoma (DLBCL) from nodal marginal zone lymphoma; **OR**
    c. Gastric MALT lymphoma; **OR**
    d. Nongastric MALT lymphoma (noncutaneous); **OR**
    e. Nodal marginal zone lymphoma; **OR**
    f. Splenic marginal zone lymphoma; **OR**
    g. DLBCL arising from follicular lymphoma; **AND**
    h. Yescarta is used for disease that is relapsed or refractory after two or more lines of systemic therapy; **OR**
    Note: Examples of systemic therapy include CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Gazyva (obinutuzumab intravenous infusion) or rituximab products, CVP (cyclophosphamide, vincristine, prednisone) + rituximab products, lenalidimide + rituximab products.
3. Patient has **ONE** of the following diagnoses:
    a. Human immunodeficiency virus (HIV) -related B-cell lymphoma; **OR**
    b. Primary effusion lymphoma**; OR**
    c. Human herpes virus 8-positive diffuse large B-cell lymphoma; **OR**
    d. Post-transplant lymphoproliferative disorders; **OR**
    e. Diffuse large B-cell lymphoma; **OR**
    f. Primary mediastinal large B-cell lymphoma; **OR**
    g. High-grade B-cell lymphoma; **OR**
    h. Large B-cell lymphoma; **AND**
    i. Yescarta is used in **ONE** of the following situations:
        i. For disease that is relapsed or refractory after two or more lines of systemic therapy; **OR**

    Note: Examples of systemic therapy include RCHOP (rituximab product, cyclophosphamide, doxorubicin, vincristine, prednisone), dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide,

doxorubicin) + rituximab product, DHA (dexamethasone, cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) ± rituximab product.

ii. For primary refractory disease; **OR**

iii. For relapsed disease < 12 months after completion of first-line therapy; **OR**

Note: Examples of first-line therapy include RCHOP (rituximab product, cyclophosphamide, doxorubicin, vincristine, prednisone), dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + rituximab product, RCDOP (rituximab product, cyclophosphamide, liposomal doxorubicin, vincristine, prednisone).

iv. For disease relapse > 12 months after first-line therapy in a patient with intent to proceed to transplantation who has partial response to second-line therapy; **AND**

Note: Examples of systemic therapy include RCHOP (rituximab product, cyclophosphamide, doxorubicin, vincristine, prednisone), dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin) + rituximab product, RCDOP (rituximab product, cyclophosphamide, liposomal doxorubicin, vincristine, prednisone).

4. Patient did not receive prior allogeneic hematopoietic stem cell transplantation (HSCT); **AND**
5. Patient received or plans to receive lymphodepleting chemotherapy prior to Yescarta infusion; **AND**
6. Patient must not be currently pregnant and sexually-active females of reproductive potential should have pregnancy status verified through a pregnancy test; **AND**
7. Patient does not have a clinically significant active systemic infection or inflammatory disorder; **AND**
8. Patient has not received live vaccines within 6 weeks prior to the start of lymphodepleting chemotherapy, during Yescarta treatment, and will not receive live vaccines until immune recovery following treatment; **AND**
9. 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**
10. Prophylaxis for infection has been followed according to local guidelines; **AND**
11. Healthcare facility has enrolled in the Yescarta REMS and training has been given to providers on the management of cytokine release syndrome (CRS) and neurological toxicities; **AND**
12. Patient will be using Yescarta (axicabtagene ciloleucel) at a treatment center that is certified to administer Yescarta (axicabtagene ciloleucel); **AND**
13. 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**
14. 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: $2 \text{ X } 10^6$ CAR-positive viable T cells per kg body weight, with a maximum of $2 \text{ X } 10^8$ CAR-positive viable T cells.

Exclusion Criteria

1. Patient has a diagnosis of primary central nervous system lymphoma
2. Patient has previously received CAR-T therapy

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
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
C85.20	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
Z85.72	Personal history of non-Hodgkin lymphomas

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	1/2/2024	Annual Review: Initial Criteria: Replaced "Acquired immune deficiency syndrome (AIDS)" with "Human immunodeficiency virus (HIV)" -related B-cell lymphoma; **OR** Added "Primary effusion lymphoma**; OR"** Removed: "Patient's disease is relapsed, or refractory defined as one of the following: a. Relapse within 1 year after autologous hematopoietic stem cell transplantation (HSCT); **OR** b. Refractory disease to the most recent therapy; **AND "**
EmblemHealth & ConnectiCare	3/6/2023	Annual Review: No Revisions
EmblemHealth & ConnectiCare	10/27/2022	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.