Drug Coverage Policy

Effective Date.....6/1/2025
Coverage Policy Number.....IP0198
Policy Title.....Yescarta

Oncology (Injectable – CAR-T) – Yescarta

- Yescarta® (axicabtagene ciloleucel intravenous infusion – Kite Pharma)

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Yescarta, a CD19-directed genetically modified autologous T-cell immunotherapy, is indicated for the treatment of adults with:[1]

- **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:
  - Disease that is refractory to first-line chemoimmunotherapy or relapses within 12 months of first-line chemoimmunotherapy.
  - 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.

Yescarta, a chimeric antigen receptor T-cell (CAR-T) therapy, is supplied as an infusion bag containing approximately 68 mL of frozen suspension of genetically modified autologous T cells.[1] Yescarta is stored in the vapor phase of liquid nitrogen (less than or equal to minus 150°C) and supplied in a liquid nitrogen dry shipper.

Guidelines
The National Comprehensive Cancer Network (NCCN) has addressed Yescarta in the following guidelines:

- **B-cell lymphoma:** Guidelines (version 2.2025 – February 10, 2025) recommend Yescarta for the treatment of a variety of B-cell lymphomas in patients with relapsed or refractory disease and after at least two chemotherapy regimens.[2,3] Recommended indications include follicular lymphoma, extranodal marginal zone lymphoma of the stomach, extranodal marginal zone lymphoma of nongastric sites (noncutaneous), nodal marginal zone lymphoma, splenic marginal zone lymphoma, DLBCL, DLBCL which transformed from indolent lymphoma, high-grade B-cell lymphoma, human immunodeficiency virus (HIV)-related B-cell lymphoma, primary effusion lymphoma, human herpes virus 8 (HHV8)-positive DLBCL, and post-transplant lymphoproliferative disorders (category 2A). In addition, Yescarta is recommended for DLBCL, high-grade B-cell lymphoma, HIV-related B-cell lymphoma, primary effusion lymphoma, HHV8-positive DLBCL, and post-transplant lymphoproliferative disorders as additional therapy for relapsed or refractory disease > 12 months after completion of first-line therapy and partial response following second-line therapy (category 2A) and for patients with primary refractory or relapsed disease < 12 months after first-line therapy (category 1 for DLBCL, category 2A for all others).
- **Pediatric aggressive mature B-cell lymphoma:** Guidelines (version 2.2024 – September 3, 2024) recommend Yescarta for relapsed or refractory primary mediastinal large B-cell lymphoma after at least two chemoimmunotherapy regimens, as consolidation/additional therapy if partial response following therapy for refractory or relapsed disease (category 2A).[3,4]

Safety
Yescarta has a Boxed Warning regarding cytokine release syndrome, neurological toxicities, and secondary hematological malignancies. Due to these risks, Yescarta is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called Yescarta REMS.[1]

Coverage Policy

Yescarta is considered medically necessary when the following criteria are met:

POLICY STATEMENT
Prior Authorization is required for medical benefit coverage of Yescarta. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Because of the specialized skills required for evaluation and diagnosis of patients treated with Yescarta, as well as the

monitoring required for adverse events and long-term efficacy, approval requires Yescarta to be prescribed by or in consultation with a physician who specializes in the condition being treated. The approval duration is 6 months to allow for an adequate time frame to prepare and administer 1 dose of therapy.

1. B-Cell Lymphoma. Approve a single dose if the patient meets ALL of the following (A, B, C, D, and E):

A) Patient is ≥ 18 years of age; AND

B) Patient meets ONE of the following (i or ii):

i. Patient meets BOTH of the following (a and b):

a) Patient has ONE of the following diagnoses [(1), (2), (3), (4), (5), or (6)]:

(1) Follicular lymphoma; OR

(2) Extranodal marginal zone lymphoma of the stomach; OR

(3) Extranodal marginal zone lymphoma of nongastric sites (noncutaneous); OR

(4) Nodal marginal zone lymphoma; OR

(5) Splenic marginal zone lymphoma; OR

(6) Diffuse large B-cell lymphoma arising from indolent lymphoma; AND

b) 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.

ii. Patient meets BOTH of the following (a and b):

a) Patient has ONE of the following diagnoses [(1), (2), (3), (4), (5), (6), (7), (8), or (9)]:

(1) Human immunodeficiency virus (HIV)-related B-cell lymphoma; OR

(2) HIV-related plasmablastic lymphoma; OR

(3) Human herpes virus 8-positive diffuse large B-cell lymphoma; OR

(4) Primary effusion lymphoma; OR

(5) Post-transplant lymphoproliferative disorders; OR

(6) Diffuse large B-cell lymphoma; OR

(7) Primary mediastinal large B-cell lymphoma; OR

(8) High-grade B-cell lymphoma; OR

(9) Large B-cell lymphoma; AND

b) Yescarta is used in ONE of the following situations [(1), (2), (3), or (4)]:

(1) 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.

(2) Primary refractory disease; OR

(3) 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).

(4) Disease relapse > 12 months after first-line therapy and 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).

C) Patient received or plans to receive lymphodepleting chemotherapy prior to Yescarta infusion; AND

D) Patient has not been previously treated with chimeric antigen receptor T-cell (CAR-T) therapy; AND
Note: Examples of CAR-T therapy includes Yescarta, Breyanzi (lisocabtagene maraleucel intravenous infusion), Kymriah (tisagenlecleucel intravenous infusion), Tecartus (brexucabtagene autoleucel intravenous infusion) Abecma (idecabtagene vicleucel intravenous infusion) and Carvykti (ciltacabtagene autoleucel intravenous infusion).

E) Yescarta is prescribed by or in consultation with an oncologist.

Dosing. The dose is up to a maximum of 2 x 10^8 CAR-positive viable T-cells administered intravenously.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Yescarta for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	**Description**
38225	Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day
38226	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (eg, cryopreservation, storage)
38227	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration
38228	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous

HCPCS Codes	Description
Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 car-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose

***Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.**

References

1. Yescarta® intravenous infusion [prescribing information]. Santa Monica, CA: Kite Pharma; June 2024.
2. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2025 – February 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 25, 2025.
3. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 25, 2025. Search term: axicabtagene.
4. The NCCN Pediatric Aggressive Mature B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2024 – September 3, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 25, 2025.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	• Changed Gastric MALT lymphoma to extranodal marginal zone lymphoma of the stomach • Changed Nongastric MALT lymphoma (noncutaneous) to extranodal marginal zone lymphoma of nongastric sites (noncutaneous) • Changed Acquired Immune Deficiency Syndrome (AIDS)-related B-cell lymphoma to Human Immunodeficiency Virus (HIV)-related B-cell lymphoma • Added Primary effusion lymphoma as an option for approval • Added dosing information for the treatment of B-cell lymphoma	4/1/2024
Annual Revision	**B-Cell Lymphoma.** Follicular was changed to indolent in the option for approval "diffuse large B-cell lymphoma arising from indolent lymphoma." Removed diffuse large B-cell lymphoma arising from nodal marginal zone lymphoma. Removed "in a patient with intent to proceed to transplantation who has" from option for approval "disease relapse > 12 months after first-line therapy and partial response to second-line therapy." **Removed** documentation from diagnosis criteria	6/1/2025

	Added HIV-related plasmablastic lymphoma as a new option for approval. **Updated CPT Coding:** **Removed CPT Codes**: 0537T, 0538T, 0539T, 0540T (Codes deleted 12/31/2024) **Added CPT Codes:** 38225, 38226, 38227, 38228 (Codes effective 1/1/2025)	

The policy effective date is in force until updated or retired.