Drug Coverage Policy

Effective Date.....4/1/2024
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 and have discretion in making individual coverage determinations. 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.

Medical Necessity Criteria

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

1. **B-Cell Lymphoma.** Individual meets **ALL** of the following criteria:
    A. Age 18 years or older
    B. Documentation of **ONE** of the following:
        i. Individual meets **BOTH** of the following:
            a. Documented diagnosis of **ONE** of the following:
                (1) Follicular lymphoma
                (2) Extranodal marginal zone lymphoma of the stomach

(3) Extranodal marginal zone lymphoma of nongastric sites (noncutaneous)
(4) Nodal marginal zone lymphoma
(5) Splenic marginal zone lymphoma
(6) Diffuse large B-cell lymphoma arising from follicular lymphoma
(7) Diffuse large B-cell lymphoma arising from nodal marginal zone lymphoma

b. Yescarta is used for disease that is relapsed or refractory after two or more lines of systemic therapy
(1) For DLBCL arising from follicular lymphoma or nodal marginal zone lymphoma, chemotherapy regimen included at least ONE anthracycline or anthracenedione-based regimen, unless contraindicated

ii. Individual meets **BOTH** of the following:
a. Documented diagnosis of **ONE** of the following:
(1) Human Immunodeficiency Virus (HIV)-related B-cell lymphoma
(2) Human herpes virus 8-positive diffuse large B-cell lymphoma
(3) Primary effusion lymphoma
(4) Post-transplant lymphoproliferative disorders
(5) Diffuse large B-cell lymphoma
(6) Primary mediastinal large B-cell lymphoma
(7) High-grade B-cell lymphoma
(8) Large B-cell lymphoma

b. Yescarta is used in **ONE** of the following situations:
(1) Disease that is relapsed or refractory after two or more lines of systemic therapy
(2) Primary refractory disease
(3) Relapsed disease less than 12 months after completion of first-line therapy
(4) Disease relapse greater than 12 months after first-line therapy in an individual with intent to proceed to transplantation who has partial response to second-line therapy

C. Has received or plans to receive lymphodepleting chemotherapy (for example, cyclophosphamide and fludarabine) prior to Yescarta infusion
D. Has not been previously treated with chimeric antigen receptor T-cell (CAR-T) therapy
E. Individual is not being treated for primary central nervous system lymphoma
F. Medication is prescribed by, or in consultation with, an oncologist or hematologist

Dosing. Up to a maximum of 2×10^8 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.

Authorization Duration

Authorization is for a single dose.

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven.

Coding/Billing 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
0537T	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
0538T	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage)
0539T	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration
0540T	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

Background

OVERVIEW
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 2.2023 – February 8, 2023) 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 grade 1 or 2, 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 follicular lymphoma or nodal marginal zone 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 3.2022 – October 19, 2022) recommend Yescarta for relapsed or refractory primary mediastinal large B-cell lymphoma after at least two chemotherapy regimens, as additional therapy for relapsed or refractory disease > 12 months after completion of first-line therapy and partial response following second-line therapy, and for patients with primary refractory or relapsed disease < 12 months after first-line therapy (category 2A).[3,4]

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

References

1. Yescarta® intravenous infusion [prescribing information]. Santa Monica, CA: Kite Pharma; November 2022.
2. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2023 – February 8, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 21, 2023.
3. The NCCN Drugs and Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 21, 2023. Search term: axicabtagene.
4. The NCCN Pediatric Aggressive Mature B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 3.2022 – October 19, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 21, 2023.

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

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