POLICY: Oncology (Injectable – CAR-T) – Yescarta Utilization Management Medical Policy
- Yescarta® (axicabtagene ciloleucel intravenous infusion – Kite Pharma)

EFFECTIVE DATE: 1/1/2020
LAST REVISION DATE: 09/16/2024

COVERAGE CRITERIA FOR: UCare Medical Assistance and Exchange Plans Only (PMAP, Connect, MSC+, MnCare, all Individual and Family Plans)

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 1.2024 – January 18, 2024) 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 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 1.2023 – April 4, 2023) 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 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]

POLICY STATEMENT
Prior Authorization is recommended 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Yescarta is recommended in those who meet the following criteria:

FDA-Approved Indication

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), or (8)]:
(1) Human immunodeficiency virus (HIV)-related B-cell lymphoma; OR
(2) Human herpes virus 8-positive diffuse large B-cell lymphoma; OR
(3) Primary effusion lymphoma; OR
(4) Post-transplant lymphoproliferative disorders; OR
(5) Diffuse large B-cell lymphoma; OR
(6) Primary mediastinal large B-cell lymphoma; OR
(7) High-grade B-cell lymphoma; OR
(8) 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.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Yescarta is not recommended in the following situations.

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Yescarta® intravenous infusion [prescribing information]. Santa Monica, CA: Kite Pharma; March 2024.
2. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 1.2024 – January 18, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 21, 2024.
3. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on March 21, 2024. Search term: axicabtagene.
4. The NCCN Pediatric Aggressive Mature B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 1.2023 – April 4, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed March 21, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**B-Cell Lymphoma:** Gastric MALT lymphoma was changed to extranodal marginal zone lymphoma of the stomach. Nongastric MALT lymphoma (noncutaneous) was changed to extranodal marginal zone lymphoma of nongastric sites (noncutaneous). Acquired immune deficiency syndrome (AIDS) was changed to human immunodeficiency virus (HIV). Primary effusion lymphoma was added as an option for approval.	03/29/2023
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."	03/27/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024