Utilization Review Policy 189B

POLICY: Oncology – Yescarta® (axicabtagene ciloleucel suspension for intravenous infusion – Kite Pharma)
EFFECTIVE DATE: 1/1/2021
LAST REVISION DATE: 04/22/2024

COVERAGE CRITERIA FOR: UCare Medicare Plans Only (UCare Medicare, UCare Medicare with M Health Fairview and North Memorial, EssentiaCare, Group Plans, MSHO, Connect + Medicare, UCare Your Choice)

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(s). The approval duration is 6 months to allow for an adequate time frame to prepare and administer 1 dose of therapy.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

Indications with a ^ below are also covered (and, if applicable, further detailed/referenced) in the corresponding Commercial Care Continuum (CC) Policy. Note: Additional criteria requirements for coverage of the same indication as outlined in the Commercial CC Policy and this Medicare Advantage CC Policy may NOT be the same.

Indications noted with eviCore are managed by eviCore healthcare for those clients who use eviCore for oncology and/or oncology-related reviews. For these indications, a prior authorization should be initiated through eviCore at www.eviCore.com.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Yescarta is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. B-Cell Lymphoma. ^ eviCore

Criteria. Approve a single dose if the patient meets ALL of the following (A, B, C, and D):

A) 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; OR

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. 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.
2. For primary refractory disease; OR
3. 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).
4. For 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).

B) The patient is ≥ 18 years of age; AND

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

D) The patient has not been previously treated with chimeric antigen receptor T-cell (CAR-T) therapy. 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).

Dosing. The dose is up to a maximum of 2 x 10^8 CAR-positive viable T-cells administered intravenously.[1]

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.
5. Centers for Medicare and Medicaid Services. National Coverage Determination (NCD) for Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24). Original effective date 8/7/2019. Implementation date 2/16/2021. Accessed April 22, 2024.

HISTORY

Type of Revision	Summary of Changes*	Date
New Policy	New Medicare Advantage Medical Policy	10/09/2019
Select revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	1/30/2020
Select revision	Added the following to the Policy Statement "Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy	04/03/2020

	may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles."	
Policy revision	**B-cell lymphoma:** Added approval criteria for diffuse large B-cell lymphoma arising from nodal marginal zone lymphoma. Revised criteria to not allow previous treatment with Kymriah.	05/04/2020
Policy revision	**B-cell lymphoma:** Added follicular lymphoma to the list of approvable diagnoses. Revised criterion: Patient has not been previously treated with Yescarta or Kymriah, to: Patient has not been previously treated with chimeric antigen receptor (CAR)-T therapy. Added Note listing all CAR-T therapies Revised dose to specify maximum dose is 2×10^8 CAR-positive T-cells and removed "per kg of body weight." **Conditions Not Recommended for Approval:** Removed Retreatment with Yescarta criteria (not needed since addressed in criteria section).	04/14/2021
Policy revision	**B-Cell Lymphoma:** Added "or plan to receive" to the requirement that the patient receive lymphodepleting chemotherapy prior to Yescarta infusion. Also, for the criterion "The patient has not been previously treated with CAR-T therapy" – added Abecma to the list of examples of CAR-T therapy.	01/14/2022
Policy revision	**B-Cell Lymphoma:** Added gastric MALT lymphoma, nongastric MALT lymphoma, nodal marginal zone lymphoma, and splenic marginal zone lymphoma as additional options of approval.	04/08/2022
Policy revision	**B-Cell Lymphoma:** Added other options for approval for diffuse large B-cell lymphoma (DLBCL), acquired immune deficiency syndrome-related B-cell lymphoma, human herpes virus 8-positive DLBCL, post-transplant lymphoproliferative disorders, DLBCL, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and large B-cell lymphoma. Approval options include primary refractory disease, disease relapse < 12 months after completion of first-line therapy, and disease relapse > 12 months after first-line therapy in a patient with intent to proceed to transplantation who has a partial response to second-line therapy.	06/28/2022
Policy 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.	05/01/2023
Policy revision	Added: "The approval duration is 6 months to allow for an adequate time frame to prepare and administer 1 dose of therapy." to the Policy Statement.	07/26/2023
Policy 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." Based on review of commercial policy revision	04/22/2024