Reference number(s)
2386-A

Standard Medicare Part B Management Yescarta

Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Yescarta	axicabtagene ciloleucel

Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications[1]

- Adult patients with large B-cell lymphoma that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy.
- Adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (NOS), primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.
- Adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

Limitations of Use

Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma.

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Compendial Uses[2]

- Histologic transformation of indolent lymphoma to DLBCL
- Human immunodeficiency virus (HIV)-related B-cell lymphomas
- Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
- Marginal zone lymphomas (MZL):
    - Extranodal MZL of the stomach (gastric mucosa associated lymphoid tissue (MALT) lymphoma)
    - Extranodal MZL of nongastric sites (nongastric MALT lymphoma)
    - Nodal MZL
    - Splenic MZL
- Pediatric primary mediastinal large B-cell lymphoma

All other indications will be assessed on an individual basis. Submissions for indications other than those listed in this criteria should be accompanied by supporting evidence from Medicare approved compendia.

Documentation

The following information must be available, upon request, for all submissions:

Chart notes or medical record documentation demonstrating failure of previous lines of therapy.

Exclusions

Coverage will not be provided for members with any of the following exclusions:

- Primary central nervous system lymphoma
- Previous treatment course with the requested medication or another CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
- ECOG performance status greater than or equal to 3 (member is not ambulatory and not capable of all self-care, confined to bed or chair more than 50% of waking hours)
- Inadequate and unstable kidney, liver, pulmonary or cardiac function
- Active hepatitis B, active hepatitis C or a clinically significant active systemic infection
- Active inflammatory disorder

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Coverage Criteria

Adult Large B-cell Lymphoma[1-5,A]

Authorization of 3 months (one dose) may be granted as treatment of B-cell lymphomas in members 18 years of age or older when either of the following criteria are met:

- The member has received prior treatment with two or more lines of systemic therapy and has any of the following B-cell lymphoma subtypes:
  - Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma
  - Histologic transformation of indolent lymphomas to DLBCL
  - Diffuse large B-cell lymphoma (DLBCL)
  - Primary mediastinal large B-cell lymphoma
  - High-grade B-cell lymphomas (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
  - Human immunodeficiency virus (HIV)-related B-cell lymphomas (including HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specific, and plasmablastic lymphoma)
  - Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
  - Follicular lymphoma
  - Extranodal marginal zone lymphoma of the stomach (gastric MALT)
  - Extranodal marginal zone lymphoma of nongastric sites (nongastric MALT)
  - Nodal marginal zone lymphoma
  - Splenic marginal zone lymphoma
- The member has received prior treatment with first-line chemoimmunotherapy and has relapsed/refractory disease any of the following B-cell lymphoma subtypes:
  - Diffuse large B-cell lymphoma (DLBCL)
  - Primary mediastinal large B-cell lymphoma
  - High-grade B-cell lymphomas (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
  - Human immunodeficiency virus (HIV)-related B-cell lymphomas (including HIV-related diffuse large B-cell lymphoma, primary effusion lymphoma, human herpesvirus 8 (HHV8)-positive diffuse large B-cell lymphoma, not otherwise specific, and plasmablastic lymphoma)
  - Monomorphic post-transplant lymphoproliferative disorder (B-cell type)

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Pediatric Primary Mediastinal Large B-cell Lymphoma[2]

Authorization of 3 months (one dose) may be granted for treatment of relapsed/refractory primary mediastinal large B-cell lymphoma in members less than 18 years of age when the member has received prior therapy with at least two prior chemoimmunotherapy regimens and achieved partial response.

Summary of Evidence

The contents of this policy were created after examining the following resources:

- The prescribing information for Yescarta.
- The available compendium
    - National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    - Micromedex DrugDex
    - American Hospital Formulary Service- Drug Information (AHFS-DI)
    - Lexi-Drugs
    - Clinical Pharmacology
- NCCN Guideline: B-cell lymphomas
- NCCN Guideline: Pediatric aggressive mature B-cell lymphomas
- National Coverage Determination: Chimeric Antigen Receptor (CAR) T-cell Therapy

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Yescarta are covered in addition to the following:

- Histologic transformation of indolent lymphoma to DLBCL
- Human immunodeficiency virus (HIV)-related B-cell lymphomas
- Monomorphic post-transplant lymphoproliferative disorder (B-cell type)
- Marginal zone lymphomas (MZL):
    - Extranodal MZL of the stomach (gastric mucosa associated lymphoid tissue (MALT) lymphoma)
    - Extranodal MZL of nongastric sites (nongastric MALT lymphoma)
    - Nodal MZL
    - Splenic MZL
- Pediatric primary mediastinal large B-cell lymphoma

Explanation of Rationale

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Yescarta to treat compendial uses in section V can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare

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Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

All FDA-approved indications are covered according to the conditions outlined in National Coverage Determination Manual section 110.24 (Chimeric Antigen Receptor [CAR] T-cell Therapy).

References

1. Yescarta [package insert]. Santa Monica, CA: Kite Pharma; June 2024.
2. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 29, 2025.
3. NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 2.2024). © 2025 National Comprehensive Cancer Network, Inc. https://www.nccn.org. Accessed April 29, 2025.
4. National Coverage Determination (NCD) for Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24-Version 1). https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=374&ncdver=1&DocID=110.24&SearchType=Advanced&bc=EAAAAAIAAAAA&. Accessed April 30, 2025.
5. Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. N Engl J Med. 2017;377(26):2531-2544.

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