Medical Drug Clinical Criteria

Subject:	Yescarta (axicabtagene ciloleucel)		
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Table of Contents

Overview

This document addresses the use of Yescarta (axicabtagene ciloleucel). Yescarta is a CD19-directed immunotherapy that is used to treat large B-cell lymphoma and follicular lymphoma.

The FDA approved indications for Yescarta include:

- Adults 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, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL from follicular lymphoma (also called transformed follicular lymphoma)
- Adults with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy.

Yescarta is a CD19-directed genetically-modified autologous T-cell immunotherapy, also known as chimeric antigen receptor (CAR) T-cell therapy. CAR T-cells are made by first collecting T-cells from the patient. The cells are then sent to a laboratory where they are genetically engineered to produce chimeric antigen receptors. The modified T-cells, now known as CAR T-cells, have the ability to better recognize an antigen (the CD19 protein) on targeted tumor cells. After the CAR T-cells have multiplied in the laboratory, they are then infused back into the patient. The modified CAR T-cells help the body's immune system better target and treat the tumor cells.

Yescarta has a black box warning for cytokine release syndrome (CRS), and should not be administered in patients with active infection or inflammatory disorders due to risk of life-threatening reactions and death. Severe or life-threatening CRS should be treated with tocilizumab with or without corticosteroids. Yescarta also has black box warning for causing neurological toxicities, which could also be severe and life-threatening. Monitoring for neurological events after administration is recommended. Due to these black box warnings, Yescarta is only available through a Risk Evaluation and Mitigation Strategy (REMS) program.

Definitions and Measures

Allogeneic cells: Harvested from a histocompatible donor.

Autologous cells: Harvested from the individual's own cells.

Bone marrow: A spongy tissue located within flat bones, including the hip and breast bones and the skull. This tissue contains stem cells, the precursors of platelets, red blood cells, and white cells.

Chemotherapy: The medical treatment of a disease, particularly cancer, with drugs or other chemicals.

Chimerism: Cell populations derived from different individuals; may be mixed or complete.

Complete Response (CR): The disappearance of all signs of cancer as a result of treatment; also called complete remission; does not indicate the cancer has been cured.

ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:

- 0 = Fully active, able to carry on all pre-disease performance without restriction

- 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, for example, light house work, office work
- 2 = Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of waking hours
- 3 = Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
- 4 = Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
- 5 = Dead

Hematopoietic stem cells: Primitive cells capable of replication and formation into mature blood cells in order to repopulate the bone marrow.

Line of Therapy:

- First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Yescarta (axicabtagene ciloleucel)

Requests for Yescarta (axicabtagene ciloleucel) for **large B-cell lymphoma** may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a histologically confirmed diagnosis of one of the following:
  A. Diffuse large B-cell lymphoma (DLBCL), not otherwise specified; **OR**
  B. High-grade B-cell lymphoma; **OR**
  C. Primary mediastinal large B-cell lymphoma; **OR**
  D. DLBCL from follicular lymphoma; **OR**
  E. Monomorphic Post-Transplant Lymphoproliferative (B-cell type) Disorders (PTLD) (NCCN 2A); **OR**
  F. AIDS-related B cell Lymphomas (NCCN 2A); **OR**
  G. Nodal Marginal Zone Lymphoma (NCCN 2A); **OR**
  H. Gastric MALT Lymphoma (NCCN 2A); **OR**
  I. Nongastric MALT Lymphoma (Noncutaneous) (NCCN 2A); **OR**
  J. Histologic Transformation of Indolent Lymphomas to DLBCL (NCCN 2A): **OR**
  K. Splenic Marginal Zone Lymphoma (NCCN 2A);

AND

III. Individual has all of the following:
  A. Relapsed or refractory disease after receiving two or more lines of systemic therapy (which may or may not include therapy supported by autologous stem cell transplant), including all of the following:
    1. An anthracycline-containing chemotherapy regimen; **AND**
    2. For CD20-positive disease, anti-CD20 monoclonal antibody, such as rituximab; **AND**
    3. For those with DLBCL from follicular lymphoma, must have chemorefractory disease after transformation to DLBCL;

  OR

  B. Relapsed or refractory disease (≤ 12 months) after first-line rituximab and anthracycline-based chemotherapy (Label, NCT03391466)

AND

IV. Individual has adequate bone marrow reserve defined by *all* of the following:
  A. Absolute neutrophil count (ANC) ≥ 1000 cells/uL; **AND**
  B. Absolute lymphocyte count (ALC) > 100 cells/uL; **AND**
  C. Platelet count ≥ 75,000 cells/uL; **AND**

V. If individual has a history of an allogeneic stem cell transplant, there are no signs of active graft versus host disease (GVHD); **AND**
VI. Individual has not received prior treatment with CAR T cell therapy or other genetically modified T-cell therapy; **AND**
VII. Individual has a current ECOG performance status of 0-1; **AND**
VIII. Individual is using as a one-time, single administration treatment.

Yescarta (axicabtagene ciloleucel) for **large B-cell lymphoma** may not be approved for the following (Label, NCT02348216):

I. Repeat administration; **OR**
II. Diagnosis of primary central nervous system lymphoma; **OR**
III. Cardiac ejection fraction (EF) less than 40%, or other clinically significant cardiac disease; **OR**
IV. Using in combination with other chemotherapy agents (not including the use of lymphodepleting chemotherapy as labeled prior to Yescarta infusion); **OR**
V. History or presence of CNS disorders such as seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, or autoimmune disease with CNS involvement~~)~~; **OR**
VI. If prescribed in combination with other CAR T-cell immunotherapy (e.g. Abecma, Breyanzi, Carvykti, Kymriah, Tecartus); **OR**
VII. Individual has active GVHD; **OR**
VIII. Active or latent hepatitis B, active hepatitis C, or other active, uncontrolled infection; **OR**
IX. When the above criteria are not met, and for all other indications.

Requests for Yescarta (axicabtagene ciloleucel) for **follicular lymphoma** may be approved if the following criteria are met:

I. Individual is 18 years of age or older; **AND**
II. Individual has a diagnosis of relapsed or refractory follicular lymphoma Grade 1, 2, or 3A; **AND**
III. Disease progression after two or more lines of systemic therapy with combination chemoimmunotherapy, including the following:
A. Anti-CD20 monoclonal antibody, such as rituximab, combined with an alkylating agent; **AND**
~~II.~~ If individual has a history of an allogeneic stem cell transplant, there are no signs of active graft versus host disease (GVHD); **AND**
IV. Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0 to 1; **AND**
V. Individual has not received prior treatment with CAR-T cell therapy or other genetically modified T-cell therapy; **AND**
VI. Individual is using as a one-time, single administration treatment.

Yescarta (axicabtagene ciloleucel) for **follicular lymphoma** may not be approved for the following (Label, NCT03105336):

I. Repeat administration; **OR**
II. Presence or history of primary central nervous system lymphoma; **OR**
III. Individual has a diagnosis of follicular lymphoma, grade 3B; **OR**
IV. History or presence of CNS disorders such as seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, or autoimmune disease with CNS involvement; **OR**
V. Diagnosis of transformed follicular lymphoma, transformed marginal zone lymphoma, small lymphocytic lymphoma, or other aggressive lymphomas; **OR**
VI. Using in combination with other chemotherapy agents (not including the use of lymphodepleting chemotherapy prior to infusion); **OR**
VII. If prescribed in combination with other CAR T-cell immunotherapy (e.g. Abecma, Breyanzi, Carvykti, Kymriah, Tecartus); **OR**
VIII. Individual has active GVHD; **OR**
IX. When the above criteria are not met, and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT

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 [for Yescarta]
0538T	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (eg, cryopreservation, storage) [for Yescarta]
0539T	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration [for Yescarta]

0540T	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous [for Yescarta]

HCPCS

Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 CAR positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose [Yescarta]

ICD-10 Procedure

XW033C7	Introduction of engineered autologous chimeric antigen receptor T-cell immunotherapy into peripheral vein, percutaneous approach, new technology group 3 [when specified as Yescarta]
XW043C7	Introduction of engineered autologous chimeric antigen receptor T-cell immunotherapy into central vein, percutaneous approach, new technology group 3 [when specified as Yescarta]

ICD-10 Diagnosis

C91.00-C91.02	Acute lymphoblastic leukemia
C82.00-C82.99	Follicular lymphoma
C83.30-C83.39	Diffuse large B-cell lymphoma
C85.20-C85.29	Mediastinal (thymic) large B-cell lymphoma
Z51.12	Encounter for antineoplastic immunotherapy

Document History

Revised: 06/12/2023
Document History:

- 06/12/2023 – Select Review: Update may not be approved criteria for Large B-cell lymphoma to remove language regarding use in those with HIV infection. Coding Reviewed: No changes.
- 11/18/2022 – Annual Review – Update criteria language to include additional B-Cell lymphomas listed as 2A recommendations from NCCN (Monomorphic PTLD, AIDS-related B cell lymphoma, Nodal Marginal Zone Lymphoma, Gastric MALT Lymphoma, Nongastric MALT Lymphoma (noncutaneous), Histologic transformation of indolent lymphomas, and splenic marginal zone lymphoma). Added criteria to specify that an individual does not have active GVHD even with a history of allogeneic stem cell transplant. Added criteria to prevent prior treatment with a CAR-T cell agent. Added criteria to the may not be approved section for cardiac ejection fracture, combination use with other CAR-T cell therapy and active GVHD. For the follicular lymphoma criteria, clarified diagnosis criteria, added criteria for those with a history of allogeneic stem cell transplant and ensure prior CAR-T cell therapy has not been used. In the may not be approved criteria, added criteria for grade 3b follicular lymphoma and combination use with other CAR T-cell therapy. Removed criteria for allogeneic stem cell transplant and history of CAR-T or other T-cell therapy. Coding Reviewed: No changes.
- 05/20/2022 – Select Review: Update criteria language to include FDA approved use as second line therapy in relapsed/refractory large B-cell lymphoma (LBCL). Coding Reviewed: No changes.
- 11/19/2021 – Annual Review: No changes. Coding reviewed: No changes.
- 05/21/2021 – Select Review: Update non-approvable criteria to remove restriction regarding cerebrospinal fluid malignant cells, or brain metastases, or [secondary] central nervous system (CNS) lymphoma in large B-cell lymphomas. Coding Reviewed: No changes. Effective 10/1/2021 Added XW033C7, XW043C7. Removed XW033C3, XW043C3.
- 03/15/2021 – Select Review: Update criteria to add new indication for follicular lymphoma per label. Wording and formatting changes. Coding Reviewed: No changes.
- 11/20/2020 – Annual Review: Update criteria to clarify that repeat administration is not approvable. Add Tecartus as an example of CAR-T therapy in non-approvable criteria. Coding Reviewed: Added ICD-10-CM C91.00-C91.02
- 05/15/2020 – Select Review: Clarify non-approvable criteria when using in combination with other chemotherapy agents. Coding review: No changes
- 11/15/2019 – Annual Review: Initial review of Yescarta (axicabtagene ciloleucel) from medical policy MED.00123. Update non-approvable criteria to exclude use in primary CNS lymphoma, and history or presence of detectable CSF malignant cells. Remove language of “any central nervous system disease” from non-approvable criteria. Clarify use in combination with other chemotherapy agents, and previous history of CAR-T agents. Coding Reviewed: No changes

References

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.