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Section:	Prescription Drugs	**Effective Date:**	January 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	November 3, 2017
Subject:	Yescarta	**Page:**	1 of 7

Last Review Date: December 8, 2023

Yescarta

Description

Yescarta (axicabtagene ciloleucel)

Background
Yescarta (axicabtagene ciloleucel) is a genetically-modified autologous T cell immunotherapy created using an individual patient's own T-cells, a type of white blood cell known as a lymphocyte. The patient's T-cells are collected and sent to a manufacturing center where they are genetically modified to include a new gene that contains a specific protein (a chimeric antigen receptor or CAR) that directs the T-cells to target and kill cancer cells that have a specific antigen (CD19) on the surface. Once the cells are modified, they are infused back into the patient to kill the cancer cells (1).

Regulatory Status
FDA-approved indications: Yescarta is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of: (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, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma
    - Limitations of Use: Yescarta is not indicated for the treatment of patients with primary central nervous system lymphoma.

- Adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy

Yescarta has a boxed warning for cytokine release syndrome (CRS) and neurological toxicities. Patients with an active infection or inflammatory disorders should not receive Yescarta and monitoring for neurological events should be done after treatment of Yescarta (1).

Yescarta is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Healthcare facilities that dispense and administer Yescarta must be enrolled and comply with the REMS requirements. Certified healthcare facilities must have on-site, immediate access to tocilizumab (Actemra), and ensure that a minimum of two doses of tocilizumab are available for each patient for administration within 2 hours after Yescarta infusion, if needed for treatment of CRS (1).

Serious infections, including life-threatening or fatal infections, occurred in patients after Yescarta infusion. Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, can occur in patients treated with drugs directed against B cells. Perform screening for HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing (1).

CD19-directed CAR-T cell therapy is supported by the National Comprehensive Cancer Network (NCCN) Guidelines for the treatment of B-cell lymphomas only after two or more chemoimmunotherapy regimens and if not previously given (2).

The safety and effectiveness of Yescarta have not been established in pediatric patients (1).

Related policies
Breyanzi, Kymriah, Tecartus

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Yescarta may be considered **medically necessary** if the conditions indicated below are met.

Yescarta may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Large B-cell lymphoma
2. Diffuse large B-cell lymphoma (DLBCL)
3. Primary mediastinal large B-cell lymphoma
4. High grade B-cell lymphoma
5. Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma

AND ALL of the following:

a. **NO** diagnosis of primary central nervous system lymphoma
b. Patient must have **ONE** of the following:
    i. Patient must have received **TWO** or more lines of systemic therapy including:
        a. Anti-CD20 monoclonal antibody for CD20-positive tumor
        b. Anthracycline-containing chemotherapy regimen
        c. Transformed follicular lymphoma **ONLY**: prior chemotherapy for follicular lymphoma and subsequently had chemorefractory disease after transformation to diffuse large B-cell lymphoma
    ii. Large B-cell lymphoma **only**: Refractory to first-line chemoimmunotherapy **OR** patient has relapsed within 12 months of first-line chemoimmunotherapy
c. Absence of active infection (including TB, HBV, HCV, and HIV)
d. Patient is not at risk for HBV infection **OR** patient is at risk for HBV infection and HBV infection has been ruled out or treatment for HBV infection has been initiated
e. Patient has adequate organ and bone marrow function as determined by the prescriber
f. Prescriber agrees to monitor the patient for signs and symptoms of cytokine release syndrome (CRS) and administer tocilizumab (Actemra) if needed
g. Prescriber agrees to monitor the patient for signs and symptoms of neurological toxicities

h. Administered in a healthcare facility enrolled in the Yescarta REMS program
i. **NO** prior therapy with any other gene therapy (e.g., Abecma, Breyanzi, Carvykti, Kymriah, Tecartus)
j. **NO** dual therapy with any other gene therapy (e.g., Abecma, Breyanzi, Carvykti, Kymriah, Tecartus)

Age 18 years of age or older

Diagnosis

Patient must have the following:

1. Follicular lymphoma

AND ALL of the following:

a. Patient must have received **TWO** or more lines of systemic therapy for treatment of follicular lymphoma
b. **NO** diagnosis of primary central nervous system lymphoma
c. Patient has adequate organ and bone marrow function as determined by the prescriber
d. Absence of active infection (including TB, HBV, HCV, and HIV)
e. Patient is not at risk for HBV infection **OR** patient is at risk for HBV infection and HBV infection has been ruled out or treatment for HBV infection has been initiated
f. Prescriber agrees to monitor the patient for signs and symptoms of cytokine release syndrome (CRS) and administer tocilizumab (Actemra) if needed
g. Prescriber agrees to monitor the patient for signs and symptoms of neurological toxicities
h. Administered in a healthcare facility enrolled in the Yescarta REMS program
i. **NO** prior therapy with any other gene therapy (e.g., Abecma, Breyanzi, Carvykti, Kymriah, Tecartus)
j. **NO** dual therapy with any other gene therapy (e.g., Abecma, Breyanzi, Carvykti, Kymriah, Tecartus)

Prior – Approval *Renewal* Requirements

None

Policy Guidelines

Pre – PA Allowance

None

Prior - Approval Limits

Quantity One infusion (only one PA approval for one infusion per lifetime)

Rationale

Summary

Yescarta is an autologous T cell immunotherapy and is intended for the treatment of certain types of lymphoma in adults who have not responded to or who have relapsed after at least two other kinds of treatment. Yescarta may cause cytokine release syndrome (CRS) and neurological toxicities. Yescarta should not be administered in patients with an active infection or any inflammatory disorders. Safety and efficacy have not been established in pediatric patients (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Yescarta while maintaining optimal therapeutic outcomes.

References

1. Yescarta [package insert]. Santa Monica, CA: Kite Pharma, Inc.; November 2022.
2. NCCN Clinical Practice Guidelines in Oncology® B-Cell Lymphomas (Version 5.2023). National Comprehensive Cancer Network, Inc. July 2023. Accessed on September 29, 2023.

Policy History

Date	Action
November 2017	Addition to PA
December 2017	Annual review
February 2018	Changed the requirement of patient has had prior autologous stem cell transplantation (ASCT) that has progressed within a year post stem cell infusion to one of the following as part of the initial therapy
March 2018	Annual editorial review

	Remove of “in bone marrow or peripheral blood” from the documentation of CD19 tumor expression requirement and removed “autologous” from stem cell transplant
August 2018	Removal of requirement: documentation of CD19 tumor expression
September 2018	Annual review Addition of specific prior lines of therapy for DLBCL and no dual therapy with another CD19-directed CAR-T cell therapy treatment or any other gene therapy per SME
June 2019	Annual review
June 2020	Annual review and reference update
December 2020	Annual editorial review
March 2021	Added the requirement: No prior therapy with another CD19-directed CAR-T cell therapy per NCCN Guidelines. Updated the REMS requirement from prescriber and patient must be enrolled to healthcare facility administering the infusion must be enrolled. Revised PA quantity limit from 1 infusion per lifetime to 1 infusion, 3 months duration. Added clarifying statement indicating that only 1 infusion/one PA approval allowed per member’s lifetime
April 2021	Addition of indication: follicular lymphoma. Revised no prior therapy and no dual therapy statements to include any other gene therapy
June 2021	Annual review and reference update
September 2021	Annual review and reference update
March 2022	Per FEP: Removal of requirement that the patient has had prior stem cell transplant. Addition of requirement for both indications that patient has adequate organ and bone marrow function as determined by the prescriber. Addition of requirement for follicular lymphoma of NO diagnosis of central nervous system lymphoma
April 2022	Per PI update, addition of indication: large B-cell lymphoma that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy
June 2022	Annual review and reference update. Addition of Carvykti to gene therapy requirement
October 2022	Per FEP, removed duration from PA
December 2022	Annual review
March 2022	Annual review and reference update
June 2023	Annual review and reference update
September 2023	Annual review and reference update

December 2023	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 8, 2023 and is effective on January 1, 2024.