Yescarta (axicabtagene ciloleucel)

Background
Yescarta is a genetically-modified autologous T cell immunotherapy indicated for the treatment of B-cell lymphoma who have not responded to or who have relapsed after at least two other kinds of treatment. Each dose of Yescarta is a customized treatment 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 indication: Yescarta is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of 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 (1).

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

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

Related policies
Kymriah

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 for use in patients 18 years of age and older with relapsed or refractory large B-cell lymphoma, diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma; and if the conditions indicated below are met.

Yescarta may be considered investigational in patients below 18 years of age and 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, as part of their initial therapy:  
   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. Patient has had prior stem cell transplantation that has progressed within a year post stem cell infusion  
   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. Prescriber agrees to monitor the patient for signs and symptoms of cytokine release syndrome (CRS) and administer tocilizumab (Actemra) if needed  
   f. Prescriber agrees to monitor the patient for signs and symptoms of neurological toxicities  
   g. Patient and prescriber are enrolled in Yescarta REMS Access program  
   h. **NO** dual therapy with another CD19-directed CAR-T cell therapy treatment (Kymriah) or any other gene therapy

**Prior – Approval Renewal Requirements**  
None
Pre – PA Allowance
None

Prior - Approval Limits

Duration One infusion per Lifetime

Rationale

Summary
Yescarta is an autologous T cell immunotherapy and is intended for of B-cell lymphoma 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 has not been established in pediatric patients (1).

References

Policy History

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<td>November 2017</td>
<td>Addition to PA</td>
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<tr>
<td>December 2017</td>
<td>Annual review</td>
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<tr>
<td>February 2018</td>
<td>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</td>
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<tr>
<td>March 2018</td>
<td>Annual editorial review</td>
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<td>Remove of “in bone marrow or peripheral blood” from the documentation of CD19 tumor expression requirement and removed “autologous” from stem cell transplant</td>
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<tr>
<td>August 2018</td>
<td>Removal of requirement: documentation of CD19 tumor expression</td>
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<td>September 2018</td>
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<td>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</td>
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June 2019 Annual review

**Keywords**

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 20, 2019 and is effective on July 1, 2019.