Oncology – Yescarta® (axicabtagene ciloleucel suspension for intravenous infusion – Kite Pharma)

APPROVAL DATE: 04/24/2019

OVERVIEW
Yescarta, a CD19-directed genetically modified autologous T cell immunotherapy, is 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 B-cell lymphoma (DLBCL) not otherwise specified, primarily mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.1 Yescarta has a Boxed Warning regarding cytokine release syndrome (CRS) 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

Yescarta is supplied as an infusion bag containing approximately 68 mL of frozen suspension of genetically modified autologous T cells in 5% DMSO and 2.5% albumin (human).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.

Clinical Efficacy
The efficacy of Yescarta was established in one single-arm, open-label, Phase II, multicenter trial that included adult patients with relapsed or refractory aggressive B-cell non-Hodgkin lymphoma (NHL) [ZUMA-1].1,2 Yescarta was given as a single infusion after lymphodepleting chemotherapy. In total, 101 of 111 patients who underwent leukapheresis received Yescarta and most (76%) had DLBCL, 16% of patients had transformed follicular lymphoma, and 8% of patients had primary mediastinal large B-cell lymphoma. The median number of prior therapies was three. The median dose was 2.0 x 10⁶ CAR-positive viable T cells.1,2

Guidelines
The National Comprehensive Cancer Network (NCCN) guidelines for B-cell lymphoma (version 2.2019 – March 6, 2019) 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.3,4 Recommended indications include DLBCL which transformed from follicular lymphoma, DLBCL, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, AIDS-related B-cell lymphoma, human herpes virus 8 (HHV8)-positive DLBCL, and post-transplant lymphoproliferative disorders.

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).

Because of the specialized skills required for evaluation and diagnosis of patients treated with Yescarta, as well as the monitoring required for adverse events and long-term efficacy, approval requires Yescarta to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Yescarta is recommended in those who meet one of the following criteria:
FDA-Approved Indications

1. **B-Cell Lymphoma.** Approve a single dose if the patient meets the following criteria (A, B, C, D, E, and F):

   A) The patient meets one of the following diagnosis (i, ii, iii, iv, vi, vii, or viii):
      1. Large B-cell lymphoma; OR
      2. Diffuse large B-cell lymphoma; OR
      3. Primary mediastinal large B-cell lymphoma; OR
      4. High-grade B-cell lymphoma; OR
      5. Diffuse large B-cell lymphoma arising from follicular lymphoma; OR
      6. AIDS-related B-cell lymphoma; OR
      7. Human herpes virus 8-positive diffuse large B-cell lymphoma; OR
      8. Post-transplant lymphoproliferative disorders; AND
   
   B) The patient is ≥ 18 years of age; AND
   
   C) Yescarta is prescribed by or in consultation with an oncologist; AND
   
   D) Yescarta is being used for disease that is relapsed or refractory after two or more lines of systemic therapy; AND
   
   E) The patient received lymphodepleting chemotherapy prior to Yescarta infusion; AND
   
   F) The patient has not been previously treated with Yescarta.

Dosing in B-Cell Lymphomas

*Dosing must meet the following:*¹ The target dose is $2 \times 10^6$ chimeric antigen receptor (CAR)-positive viable T cells per kg body weight administered intravenously, with a maximum of $2 \times 10^8$ CAR-positive viable T-cells.

**CONDITIONS NOT RECOMMENDED FOR APPROVAL**

Yescarta has not been shown to be effective or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. **Re-treatment with Yescarta.** Yescarta is for one time use, repeat dosing is not approvable.

2. 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™ suspension for intravenous infusion [prescribing information]. Santa Monica, CA: Kite Pharma; October 2017.

**HISTORY**

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes*</th>
<th>Approval Date</th>
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<tr>
<td>New Policy</td>
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<td>04/25/2018</td>
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<tr>
<td>Annual Revision</td>
<td><strong>B-cell lymphoma:</strong> AIDS-related B-cell lymphoma, HHV8-positive DLBCL, and post-transplant lymphoproliferative disorders</td>
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04/24/2019
were added to the list of approved diagnoses. Criteria were added such that the lifetime therapy is for one dose.