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

DATE REVIEWED: 04/29/2020

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 2.0×10^6 CAR-positive viable T cells.[1-2]

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for B-cell lymphoma (version 1.2020 – January 22, 2020) 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 or nodal marginal zone 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 (category 2A).

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 diagnoses (i, ii, iii, iv, v, vi, vii, viii, or ix):
     - **i.** Large B-cell lymphoma; OR
     - **ii.** Diffuse large B-cell lymphoma; OR
     - **iii.** Primary mediastinal large B-cell lymphoma; OR
     - **iv.** High-grade B-cell lymphoma; OR
     - **v.** Diffuse large B-cell lymphoma arising from follicular lymphoma; OR
     - **vi.** Diffuse large B-cell lymphoma arising from nodal marginal zone lymphoma; OR
     - **vii.** AIDS-related B-cell lymphoma; OR
     - **viii.** Human herpes virus 8-positive diffuse large B-cell lymphoma; OR
     - **ix.** 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 or Kymriah® (tisagenlecleucel injection).

   Dosing. The dose is up to 2 x 10^8 CAR-positive viable T-cells per kg of body weight administered intravenously.[1]

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; May 2019.
2. 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.
3. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 1.2020 – January 22, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed April 17, 2020.
4. The NCCN Drugs and Biologics Compendium. © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on April 17, 2020. Search term: axicabtagene.

HISTORY

Type of Revision	Summary of Changes	Date Reviewed
New Policy	-	04/25/2018
Annual Revision	**B-cell lymphoma:** AIDS-related B-cell lymphoma, HHV8-positive DLBCL, and post-transplant lymphoproliferative disorders were added to the list of approved diagnoses. Criteria were added such that the lifetime therapy is for one dose.	04/24/2019
Annual Revision	**B-cell lymphoma:** Added approval criteria for diffuse large B-cell lymphoma arising from nodal marginal zone lymphoma. Revised criteria to not allow previous treatment with Kymriah.	04/29/2020