



# Chimeric Antigen Receptor T-cell Therapy

Clinical Guideline

Effective September 1, 2020

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# Chimeric Antigen Receptor T-cell (CAR T) Therapy

## Introduction

Chimeric antigen receptor (CAR) T-cell therapy is an adoptive T-cell therapy that uses engineered T-cell from a patient's own immune system to attack cancer cells by targeting proteins expressed on the cellular membrane. The process involves obtaining T-cells via a leukapheresis procedure. The cells are sent to a centralized manufacturing facility where they are genetically modified to produce specific chimeric antigen receptors and expanded in a cell culture. This process may take up to several weeks. The product is then returned to the treating facility and re-infused into the patient (Srivastava & Riddell, 2018).

CAR T-cell therapy has shown impressive results in clinical trials in treating various hematologic malignancies (Wang et al., 2019). The trials have demonstrated impressive response rates with durable remissions in heavily pretreated individuals (Berdeja et al., 2017). There are many other areas of active investigation using this technology to treat other malignancies (Schmidts & Maus, 2018).

The treatment is associated with the occurrence of several specific toxicities including cytokine release syndrome (CRS) and CAR - T associated neurotoxicity. The CRS is characterized by the rapid release of large amounts of cytokines into the blood after some types of immunotherapy. It is associated with fever, nausea, headache, rash, rapid heart rate, hypotension and dyspnea. It can range from a mild reaction to a severe life-threatening event. Treatment ranges from purely supportive to the use of an Il-6 antagonist such as tocilizumab. Neurologic toxicity is also observed and can range from mild to severe life-threatening events. Its pathophysiology is not adequately understood at the present time. Treatment is supportive in nature along with the use of steroids (Neelapu et al., 2018)

The purpose of this guideline is to identify the indications for CAR T-cell therapy.

## FDA-approved Agents

KYMRIAH™ (tisagenlecleucel) is a CD19-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse; 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, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma.

YESCARTA™ (axicabtagene ciloleucel) 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.

TECARTUS™ (brexucabtagene autoleucel, formerly KTE-X19) is a CD19-directed genetically modified autologous T cell immunotherapy agent indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) that received FDA approval July 24, 2020. This indication is approved under accelerated approval based on overall response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical

benefit in a confirmatory trial. TECARTUS™ utilizes a patient's own T cells that are harvested and genetically modified ex vivo by retroviral transduction to express a chimeric antigen receptor (CAR) comprising a murine anti-CD19 single-chain variable fragment (scFv) linked to CD28 and CD3-zeta co-stimulatory domains.

## Indications

KYMRIAH™ (tisagenlecleucel) is considered medically necessary when:

The member is 25 years of age or younger with a B-cell precursor acute lymphoblastic leukemia and the following criteria are met:

- The B-cells are CD19 positive
- The disease is refractory to treatment or in its second or greater relapse
- The member has not received a prior treatment with KYMRIAH™ (tisagenlecleucel)
- The member does not have active, uncontrolled CNS disease
- The member does not have:
  - o HIV, active Hepatitis B or C infection
  - o active uncontrolled infection
  - o autoimmune disease requiring immunosuppression
- For members with a history of an allogeneic Hematopoietic Stem Cell Transplant (HSCT), there is no evidence of active Graft vs Host Disease (GVHD) requiring treatment
- The treating facility is certified under the KYMRIAH™ Risk Evaluation and Mitigation Strategy (REMS) System Program <https://www.us.kymriah.com/treatment-center-locator/>

The member is 18 years of age or older diagnosed with large B-cell lymphoma including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma or DLBCL arising from follicular lymphoma

- The tumor is CD19 positive
- The member has received two or more lines of systemic therapy
- For diffuse large B-cell lymphoma arising from follicular lymphoma: member received prior treatment with two or more chemoimmunotherapy regimens which included at least one anthracycline or anthracenedione-based regimen, unless contraindicated.
- The member has not received prior treatment with KYMRIAH™ (tisagenlecleucel) or YESCARTA™ (axicabtagene ciloleucel)
- The member does not have a primary CNS lymphoma
- The member does not have:
  - o HIV, active Hepatitis B or C infection
  - o active uncontrolled infection
  - o autoimmune disease requiring immunosuppression
- For patients with a history of an allogeneic Hematopoietic Stem Cell Transplant (HSCT), there is no evidence of active Graft vs Host Disease (GVHD) requiring treatment
- The treating facility is certified under the KYMRIAH™ Risk Evaluation and Mitigation Strategy (REMS) System Program <https://www.us.kymriah.com/treatment-center-locator/>

YESCARTA™ (axicabtagene ciloleucel) is considered medically necessary when:

The member is 18 years of age or older diagnosed with large B-cell lymphoma including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma or DLBCL arising from follicular lymphoma

- The Tumor is CD19 positive
- The member has received two or more lines of systemic therapy
- For diffuse large B-cell lymphoma arising from follicular lymphoma: member received prior treatment with two or more chemoimmunotherapy regimens which included at least one anthracycline or anthracenedione-based regimen, unless contraindicated
- The member had not received prior treatment with KYMRIA™ (tisagenlecleucel) or YESCARTA™ (axicabtagene ciloleucel)
- The member does not have a primary CNS lymphoma
- The member does not have:
  - o HIV, active Hepatitis B or C infection
  - o Active uncontrolled infection
  - o Autoimmune disease requiring immunosuppression
- For patients with a history of an allogeneic Hematopoietic Stem Cell Transplant (HSCT), there is no evidence of active Graft vs Host Disease requiring treatment (GVHD)
- The treating facility is certified under the YESCARTA™ Risk Evaluation and Mitigation Strategy (REMS) System Program <https://www.yescarta.com/treatment-centers>

TECARTUS™ (brexucabtagene autoleucel) is considered medically necessary when:

- The member is 18 years of age or older
- Has a diagnosis of Mantle cell lymphoma that has either relapsed or is refractory to a first-line systemic treatment
- The Tumor is CD19 positive
- The member has not received prior treatment with Tecartus™ (brexucabtagene autoleucel)
- The member does not have:
  - o HIV, active Hepatitis B or C Infection
  - o Active, uncontrolled infection
  - o Autoimmune disease requiring immunosuppression
- The member does not have primary CNS Lymphoma
- The treating facility is certified under the Tecartus™ Risk Evaluation and Mitigation Strategy (REMS) System Program [https://www.tecartus.com/?gclid=EAlaIQobChMI2t7WktO06wIVzMDACh0LfQRHEAAYASAAEgJdRPD\\_BwE](https://www.tecartus.com/?gclid=EAlaIQobChMI2t7WktO06wIVzMDACh0LfQRHEAAYASAAEgJdRPD_BwE)

## Note

Optum believes facilities offering treatment with KYMRIA™ (tisagenlecleucel), YESCARTA™ (axicabtagene ciloleucel), or TECARTUS™ (brexucabtagene autoleucel) should be certified or in the process of obtaining certification in meeting Immune Effector Cell (IEC) standards by The Foundation for the Accreditation of Cellular Therapy (FACT).

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<b>Review and Approval History</b>	
<b>Version</b>	<b>Description of Activity</b>
1.0	06/15/2020: Reviewed by Optum Hematopoietic Stem Cell Transplant Expert Panel
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