Protocol for Chimeric Antigen Receptor (CAR) T-cell Products

Approved July 2023

Abecma® (idecabtagene vicleucel)
Breyanzi® (lisocabtagene maraleucel)
Carvykti® (ciltacabtagene autoleucel)
Kymriah® (tisagenleleucel)
Tecartus® (brexucabtagene autoleucel)
Yescarta® (axicabtagene ciloleucel)

Background: *Chimeric Antigen Receptor (CAR)-T cell therapy is a targeted, personalized therapy that contains patients' autologous T cells reengineered to fight cancer. T cell therapy is approved by the Food and Drug Administration (FDA) to treat certain types of leukemia, lymphoma, and most recently, myeloma.*

Criteria for approval:

1. Medication is prescribed by or in consultation with an oncologist, hematologist, or other specialist in the treatment of the specified disease; **AND**
2. Diagnosis has been confirmed using appropriate tests e.g., histology for Non-Hodgkin Lymphoma (NHL); immunophenotyping for Acute lymphocytic leukemia (ALL), etc., prior to initiating therapy
3. Patient is not currently pregnant; **AND**
4. Patient has no previous history of CAR-T cell therapy; **AND**
5. Patient has no active infections or inflammatory disorders
6. The treating facility is certified under the Risk Evaluation and Mitigation Strategy (REMS) System program appropriate for the requested CAR-T product.
7. Patient is educated on possible drug specific severe adverse reactions with treatment like Cytokine Release Syndrome (CRS), neurologic toxicities, etc.
8. Treatment is one time
9. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence

For Abecma:

1. Patient is 18 years or older or age is appropriate based on National Comprehensive Cancer Network (NCCN) compendium 2B or better off-label recommendation; **AND**

2. The request meets ONE of the following:
    a. Documented diagnosis of relapsed or refractory multiple myeloma; **AND** Documentation of four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody **OR**
    b. Request meets NCCN compendium 2B or better off-label recommendations

For Breyanzi:

1. Patient is 18 years or older or age is appropriate based on NCCN compendium 2B or better off- label recommendation; **AND**
    a. Documented diagnosis of large B-cell lymphoma (LBCL), including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B, who have:
        i. Refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first line chemoimmunotherapy; or
        ii. Refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for hematopoietic stem cell transplantation (HSCT) due to comorbidities or age; or
        iii. Relapsed or refractory disease after two or more lines of systemic therapy **OR**
    b. Request meets NCCN compendium 2B or better off-label recommendations

For Carvykti:

1. Patient is 18 years or older or age is appropriate based on NCCN compendium 2B or better off- label recommendation; **AND**
2. The request meets ONE of the following:
    a. Documented diagnosis of relapsed or refractory multiple myeloma; **AND** Documentation of four or more prior lines of therapy, including and immunomodulatory agent, a proteasome inhibitor, and anti-CD38 monoclonal antibody **OR**
    b. Request meets NCCN compendium 2B or better off-label recommendations

For Kymriah:

1. The request meets ONE of the following:
    a. Patient is up to 25 years old with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse **OR**
    b. Patient is 18 years or older 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 **OR**

c. Patient is 18 years or older with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.
d. Request meets NCCN compendium 2B or better off-label recommendations

For Tecartus:

1. Patient is 18 years or older or age is appropriate based on NCCN compendium 2B or better off- label recommendation; **AND**
2. The request meets one of the following:
    a. Documented diagnosis of relapsed or refractory mantle cell lymphoma (MCL) **OR**
    b. Documented diagnosis of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) **OR**
    c. Request meets NCCN compendium 2B or better off-label recommendations

For Yescarta:

1. Patient is 18 years or older or age is appropriate based on NCCN compendium 2B or better off- label recommendation; **AND**
2. The request meets ONE of the following:
    a. Patient has large B-cell lymphoma that is refractory to first line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy **OR**
    b. Patient has ANY of the following diagnosis that has not responded to or have relapsed following two or more lines of systemic therapy:
        i. Diffuse large B-cell lymphoma (DLBCL) not otherwise specified
        ii. Primary mediastinal large B-cell lymphoma
        iii. High grade B-cell lymphoma
        iv. DLBCL arising from follicular lymphoma **OR**
    c. Patient has relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy **OR**
    d. Request meets NCCN compendium 2B or better off-label recommendations

Approval Duration: One time only

References:

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2. Carvykti [package insert]. Janssen Biotech, Inc. Horsham, PA. February 2023
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4. Tecartus [package insert]. Kite Pharma, Inc. Santa Monica, CA. October 2021
5. Yescarta [package insert]. Kite Pharma, Inc. Santa Monica, CA. November 2022

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7. National Cancer Institute. CAR T-Cells: Engineering Patients' Immune Cells to Treat Their Cancers. March 10, 2022. Accessed online: May 5, 2023. https://www.cancer.gov/about- cancer/treatment/research/car-t-cells
8. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2021. Updated periodically
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