Addendum to Protocol for Chimeric Antigen Receptor (CAR) T Cell Products
July 2025

DURB Approval Dates	**7/2023, 7/2025**
Commissioners Approval Dates	**7/2024**

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

Protocol applies to FDA approved biosimilars and related indications and dosages

Addendum: The purpose of the addendum is to remove the criteria referencing the risk evaluation and mitigation strategies (REMS) program. The REMS program for chimeric antigen receptor T cell therapy was eliminated by the Food and Drug Administration (FDA). In addition, the Breyanzi criteria has been updated to include new FDA-approved indications. Criteria pertaining to age and contraindications have been added to the protocol.

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. Patient is of the FDA-labeled or compendial approved age
2. Patient does not have any contraindications to therapy
3. Medication is prescribed by or in consultation with an oncologist, hematologist, or other specialist in the treatment of the specified disease
4. 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
5. Patient is not currently pregnant
6. Patient has no previous history of CAR T cell therapy
7. Patient has no active infections or inflammatory disorders
8. Treatment is one time

9. The medication requested is prescribed in accordance with Food and Drug Administration (FDA) established indications and dosing regimens or in accordance with a 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

10. For Abecma requests patient meets i. and ii.:
    i. Documentation is received of relapsed or refractory multiple myeloma
    ii. Documentation is received of trial of at least two prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody

11. For Breyanzi requests patient meets one of the following (i. ii. iii. or iv.):
    i. Documentation is received 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 grade 3B AND meets one of the following (a. b. or c.):
        a. Refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy
        b. Refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and is not eligible for hematopoietic stem cell transplantation (HSCT)
        c. Relapsed or refractory disease after 2 or more lines of systemic therapy
    ii. Documentation is received of relapsed or refractory chronic lymphocytic leukemia or small lymphocytic lymphoma who have received at least two prior lines of therapy including, a Bruton tyrosine kinase inhibitor and a B-cell lymphoma 2 (BCL-2) inhibitor
    iii. Documentation is received of relapsed or refractory follicular lymphoma who have received 2 or more prior lines of systemic therapy
    iv. Documentation is received of relapsed or refractory mantle cell lymphoma who have received at least 2 prior lines of systemic therapy, including a Bruton tyrosine kinase inhibitor

12. For Carvykti requests patient meets all of the following (i. ii. and iii.):
    i. Documentation is received of relapsed or refractory multiple myeloma
    ii. Documentation is received of trial of at least one prior line of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody
    iii. Documentation is received patient is refractory to lenalidomide treatment

13. For Kymriah requests the patient meets one of the following (i. ii. or iii.):
    i. Documentation received of B-cell precursor acute lymphoblastic leukemia that is refractory or in second or later relapse in patients up to 25 years of

age
   ii. Documentation received of relapsed or refractory large B-cell lymphoma (including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma) after two or more lines of systemic therapy
   iii. Documentation is received of relapsed or refractory follicular lymphoma after two or more lines of systemic therapy

14. For Tecartus requests the patient meets i. or ii.:
   i. Documentation is received of relapsed or refractory mantle cell lymphoma
   ii. Documentation is received of relapsed or refractory B-cell precursor acute lymphoblastic leukemia

15. For Yescarta requests patient meets one of the following (i. ii. or iii.):
   i. Documentation is received of large B-cell lymphoma that is refractory to 1st line chemoimmunotherapy or that relapses within 12 months of 1st line chemotherapy
   ii. Documentation is received of relapsed or refractory large B-cell lymphoma (includes 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) after two or more lines of systemic therapy
   iii. Documentation is received of relapsed or refractory follicular lymphoma after two or more lines of systemic therapy

Note:
There is BOXED WARNING of Cytokine Release Syndrome, Neurologic Toxicities, Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), Prolonged Cytopenia, and Secondary Hematological Malignancies for Abecma.

There is BOXED WARNING of Cytokine Release Syndrome, Neurologic Toxicities, Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), Recurrent Cytopenia, and Secondary Hematological Malignancies for Carvykti.

There is a BOXED WARNING of Cytokine Release Syndrome, Neurologic Toxicities, and Secondary Hematological Malignancies for Yescarta, Tecartus, Breyanzi, and Kymriah.

Approval Duration: One Time Only

References:

1. Abecma [package insert]. Bristol-Myers Squibb Company. Summit, NJ. June 2025.
2. Carvykti [package insert]. Janssen Biotech, Inc. Horsham, PA. June 2025.
3. Kymriah [package insert]. Novartis Pharmaceuticals Corp. East Hanover, NJ. June 2025.
4. Tecartus [package insert]. Kite Pharma, Inc. Santa Monica, CA. June 2025.
5. Yescarta [package insert]. Kite Pharma, Inc. Santa Monica, CA. June 2024.
6. Breyanzi [package insert]. Bristol-Myers Squibb Company. Summit, NJ. June 2025.
7. Clinical Pharmacology. Gold Standard Series [Internet database]. Tampa, FL. Elsevier 2021. Updated Periodically
8. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Multiple Myeloma. Version 1.2026. Last accessed 7/7/2025.

9. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. B-Cell Lymphomas. Version 2.2025. Last accessed 7/7/2025.
10. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Acute Lymphoblastic Leukemia. Version 2.2025. Last accessed 7/72025.
11. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 3.2025. Last accessed 7/7/2025.
12. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Pediatric Acute Lymphoblastic Leukemia. Version 3.2025. Last accessed 7/7/2025.
13. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology. Pediatric Aggressive Mature B-Cell Lymphomas. Version 2.2025. Last accessed 7/7/2025.
14. Hayden PJ, Roddie C, Bader P., et al. Management of adults and children receiving CAR T cell therapy: 2021 best practice recommendations of the European Society for Blood and Marrow Transplantation (EBMT) and the Joint Accreditation Committee of ISCT and EBMT (JACIE) and the European Haematology Association (EHA). Annals of Oncology. March 2022. Vol 33 (3) p259-27.
15. US Food and Drug Administration. FDA Eliminated Risk Evaluation and Mitigation Strategies (REMS) for Autologous Chimeric Antigen Receptor CAR T cell Immunotherapies. FDA News Release. June 27, 2025. Accessed 7/7/2025. FDA Eliminates Risk Evaluation and Mitigation Strategies (REMS) for Autologous Chimeric Antigen Receptor CAR T cell Immunotherapies | FDA
16. 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