

EVH Clinical Guideline 2723.CC for CAR T-Cell Therapy

Guideline Number: EVH_CG_2723.CC	<u>Applicable Codes</u>	
<i>"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc. © 2021 - 2026 Evolent. All rights Reserved.</i>		
Original Date: October 12, 2021	Last Revised Date: August 20, 2026	Implementation Date: September 1, 2026

TABLE OF CONTENTS

STATEMENT	2
GENERAL INFORMATION	2
COVERAGE.....	2
INDICATIONS FOR IMMUNE EFFECTOR CELL THERAPY (IECT).....	2
TISAGENLECLEUCEL (KYMRIAH).....	2
AXICABTAGENE CILOLEUCEL (YESCARTA).....	3
BREXUCABTAGENE AUTOLEUCEL (TECARTUS)	4
LISOCABTAGENE MARALEUCEL (BREYANZI)	4
IDECABTAGENE VICLEUCEL (ABECMA).....	5
CILTACABTAGENE AUTOLEUCEL (CARVYKTI).....	6
OBECABTAGENE AUTOLEUCEL (AUCATZYL).....	6
LIMITATIONS	6
CODING AND STANDARDS	7
CODES.....	7
APPLICABLE LINES OF BUSINESS	8
POLICY HISTORY	8
LEGAL AND COMPLIANCE	9
GUIDELINE APPROVAL	9
Committee	9
DISCLAIMER	9
REFERENCES.....	10

STATEMENT

General Information

- *It is an expectation that all members receive care/services from a licensed clinician. All appropriate supporting documentation, including recent pertinent office visit notes, laboratory data, and results of any special testing must be provided. If applicable: All prior relevant imaging results and the reason that alternative imaging cannot be performed must be included in the documentation submitted.*
- *Where a specific clinical indication is not directly addressed in this guideline, medical necessity determination will be made based on widely accepted standard of care criteria. These criteria are supported by evidence-based or peer-reviewed sources such as medical literature, societal guidelines, and state/national recommendations.*
- *The guideline criteria in the following sections were developed utilizing evidence-based and peer-reviewed resources from medical publications and societal organization guidelines as well as from widely accepted standard of care, best practice recommendations.*

COVERAGE

This policy includes:

- Tisagenlecleucel (Kymriah)
- Axicabtagene Ciloleucel (Yescarta)
- Brexucabtagene Autoleucel (Tecartus)
- Lisocabtagene Maraleucel (Breyanzi)
- Idecabtagene Vicleucel (Abecma)
- Ciltacabtagene Autoleucel (Carvykti)
- Obecabtagene Autoleucel (Aucatzyl)

INDICATIONS FOR IMMUNE EFFECTOR CELL THERAPY (IECT) ⁽¹⁾

Tisagenlecleucel (Kymriah) ⁽²⁾

- KYMRIA is a CD19-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of:
 - Pediatric and young adult members (up to 25 years of age) with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse
 - Members have experienced disease relapse after allogeneic stem cell

transplantation (SCT) and member is ≥ 6 months from above transplantation at the time of infusion; **OR**

- Members have relapsed/refractory Philadelphia chromosome-negative B-ALL that has progressed after 2 cycles of a standard chemotherapy regimen for initial diagnosis or after 1 cycle of standard chemotherapy for relapsed leukemia; **OR**
- Members have relapsed/refractory Philadelphia chromosome-positive B-ALL that has progressed after failure of 2 prior regimens, including a Tyrosine Kinase Inhibitor (TKI)-containing regimen
- Adult members with relapsed or refractory (r/r) 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
 - Members must have previously received at least two lines of therapy (including rituximab and an anthracycline (for DLBCL)) **AND**
 - Either having failed autologous hematopoietic stem cell transplantation (HSCT) or being ineligible for or not consenting to HSCT
- Adult members with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy (including an anti-CD20 antibody and an alkylating agent) OR autologous HSCT. This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s)
- Members must present CD19 tumor expression
- Members must not have received prior CD19-directed chimeric antigen receptor (CAR) T-cell therapy
- Delay tisagenlecleucel infusion if member has unresolved serious adverse reaction from preceding chemotherapies (e.g., pulmonary reactions, cardiac reactions, hypotension), active uncontrolled infection, active graft versus host disease (GVHD), or worsening of leukemia burden following lymphodepleting chemotherapy

NOTE: Risk of using Tisagenlecleucel include cytokine release syndrome (CRS), neurological toxicities, hemophagocytic lymphohistiocytosis (HLH)/macrophage activation syndrome (MAS), hypersensitivity, infections, prolonged cytopenias, hypogammaglobulinemia, and secondary malignancies.

Axicabtagene Ciloleucel (Yescarta) ⁽³⁾

- YESCARTA is a CD19-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of:
 - Adult members (18 years of age or older) with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy or disease progression or relapse less ≤ 12 months after autologous HSCT; including DLBCL not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma

- Adult members with large B-cell lymphoma that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy
- Adult members with relapsed or refractory FL after two or more lines of systemic therapy that must have included a combination of anti-CD20 monoclonal antibody (e.g. rituximab); and an alkylating agent (eg, bendamustine, cyclophamide) containing regimen; or disease progression or relapse less ≤12 months after autologous HSCT. This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s)
- Members must present CD19 tumor expression
- Members must not have received prior CD19-directed chimeric antigen receptor (CAR) T-cell therapy
- Members must not have evidence of active infection or inflammatory disorders

NOTE: Risk of using Axicabtagene ciloleucel (Yescarta) CRS, neurological toxicities, hypersensitivity, infections, prolonged cytopenias, hypogammaglobulinemia, and secondary malignancies.

Brexucabtagene Autoleucel (Tecartus) ⁽⁴⁾

- TECARTUS is a CD19-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of:
 - Adult members (18 years of age and above) with relapsed or refractory mantle cell lymphoma (MCL) who had previously received the following treatments, but are not limited to:
 - Anthracycline or bendamustine-containing chemotherapy
 - Anti-CD20 monoclonal antibody therapy (e.g., rituximab)
 - Bruton tyrosine kinase inhibitor (BTKi) therapy (e.g., ibrutinib, acalabrutinib, zanubrutinib)
 - Adult members with relapsed or refractory B-cell precursor ALL
- Members must present CD19 tumor expression
- Members must not have received prior CD19-directed chimeric antigen receptor (CAR) T-cell therapy
- Members must not have evidence of active infection or inflammatory disorders

NOTE: Risk of using Brexucabtagene autoleucel include CRS, neurological toxicities, hemophagocytic lymphohistiocytosis/macrophage activation syndrome, hypersensitivity, infections, prolonged cytopenias, hypogammaglobulinemia, and secondary malignancies.

Lisocabtagene maraleucel (Breyanzi) ⁽⁵⁾

- BREYANZI is a CD19-directed genetically modified autologous T-cell immunotherapy

indicated for the treatment of:

- Adult members with large B-cell lymphoma, including 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 EITHER have:
 - Refractory disease to first-line chemoimmunotherapy or relapse within 12 months of first-line chemoimmunotherapy
 - Refractory disease to first-line chemoimmunotherapy or relapse after first-line chemoimmunotherapy and are not eligible for HSCT due to comorbidities or age
 - Relapsed or refractory disease after 2 or more lines of systemic therapy
- Adult members with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who have received at least 2 prior lines of therapy, including BTKi and B-cell lymphoma 2 (BCL-2) inhibitor. This indication is approved under accelerated approval based on response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s)
- Adult members with relapsed or refractory FL who have received 2 or more prior lines of systemic therapy
- Adult members with relapsed or refractory MCL who have received at least 2 prior lines of systemic therapy, including BTKi
- Adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least 2 prior lines of systemic therapy
- Delay lisocabtagene maraleucel infusion if member has unresolved serious adverse reaction from preceding chemotherapies, active uncontrolled infection, or active graft versus host disease (GVHD)
- Members must present CD19 tumor expression
- Members must not have received prior CD19-directed chimeric antigen receptor (CAR) T-cell therapy.

NOTE: Risk of using Lisocabtagene maraleucel (Breyanzi(R)) includes CRS, neurologic toxicities, hypersensitivity, infections, prolonged cytopenias, hypogammaglobulinemia, secondary malignancies, and immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome (IEC-HS).

Idecabtagene vicleucel (Abecma) ⁽⁶⁾

- ABECMA is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of adult members with relapsed or refractory multiple myeloma after two or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody
- Delay idecabtagene vicleucel for up to 7 days if member has unresolved serious adverse events (especially pulmonary events, cardiac events, or hypotension), including those

after preceding chemotherapies OR if member has active infections or inflammatory disorders

- Members must not have received prior chimeric antigen receptor (CAR) T-cell therapy

NOTE: Risk of using Idecabtagene vicleucel include early death, CRS, neurological toxicities, HLH/MAS, hypersensitivity, infections, prolonged cytopenias, hypogammaglobulinemia, and secondary malignancies.

Ciltacabtagene autoleucel (Carvykti) ⁽⁷⁾

- CARVYKTI is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of adult members with relapsed or refractory multiple myeloma after at least one prior line of therapy, including a proteasome inhibitor and an immunomodulatory agent, and are refractory to lenalidomide
- Delay ciltacabtagene autoleucel if member has ANY of the following conditions:
 - Clinically significant active infection or inflammatory disorders
 - Grade ≥ 3 non-hematologic toxicities of cyclophosphamide and fludarabine conditioning, except for Grade 3 nausea, vomiting, diarrhea, or constipation. CARVYKTI infusion should be delayed until resolution of these events to Grade ≤ 1

NOTE: Risk of using Ciltacabtagene autoleucel include early mortality, CRS, neurologic toxicities (eg, ICANS, Parkinsonism, Guillain-Barré syndrome, immune mediated myelitis, peripheral neuropathy, cranial nerve palsies), HLH/MAS, prolonged and recurrent cytopenias, infections, hypogammaglobulinemia, hypersensitivity, immune effector cell-associated enterocolitis, and secondary malignancies.

Obecabtagene Autoleucel (Aucatzyl) ⁽⁸⁾

- AUCATZYL is a genetically modified T-cell immunotherapy indicated for the treatment of adult members with relapsed or refractory B-cell precursor ALL
- Delay AUCATZYL treatment if the member is experiencing severe intercurrent infection
 - If the member requires supplementary oxygen, AUCATZYL should only be infused if considered appropriate based on the treating physician's benefit/risk assessment
 - A delay to the second split may be required to manage toxicities

NOTE: Risk of using Obecabtagene Autoleucel includes CRS, neurologic toxicities (eg, immune effector cell-associated neurotoxicity syndrome (ICANS)), prolonged cytopenias, infections, hypogammaglobulinemia, HLH/MAS, hypersensitivity, and secondary malignancies.

LIMITATIONS

- KYMRIA is not indicated for treatment of members with primary central nervous system lymphoma ⁽²⁾

- BREYANZI is not indicated for the treatment of members with primary central nervous system lymphoma ⁽⁵⁾
- CAR T-Cell Therapy is authorized once per lifetime

CODING AND STANDARDS

Codes

Code	Description
C9399	Unclassified drugs or biologicals
J3590	Unclassified biologics
J9999	Not otherwise classified, antineoplastic drugs
Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 CAR positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2042	Tisagenlecleucel, up to 600 million CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2053	Brexucabtagene autoleucel, up to 200 million autologous anti-CD19 CAR positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2054	Lisocabtagene maraleucel, up to 110 million autologous anti-CD19 CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2055	Idecabtagene vicleucel, up to 510 million autologous B-cell maturation antigen (BCMA) directed CAR-positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2056	Ciltacabtagene autoleucel, up to 100 million autologous B-cell maturation antigen (BCMA) directed CAR-positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2058	Obecabtagene autoleucel, 10 up to 400 million CD19 CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per infusion
S2107	Adoptive immunotherapy i.e., development of specific antitumor reactivity (e.g., tumor-infiltrating lymphocyte therapy) per course of treatment

Code	Description
38225	Chimeric antigen receptor T-cell (CAR-T) therapy; harvesting of blood-derived T lymphocytes for development of genetically modified autologous CAR-T cells, per day
38226	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage)
38227	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration
38228	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☐	Commercial
☐	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
August 20, 2026	Updated Guideline name; formatting updates throughout; replaced "Indications" heading with "Coverage"; updated in-text citations; updated Indications and Notes under each drug; updated description of procedure code C9399, Q2041, Q2042, Q2055 and reordered codes; removed Background Section; updated References
November 20, 2025	- This guideline replaces PA.216.CC Car-T Therapy - Editorial changes to match the formatting and layout of the new template, no changes to clinical content

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Administrative Services Medical Policy Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

This guideline is the proprietary information of Evolent. Any sale, copying, or dissemination of said policies is prohibited.

REFERENCES

1. Kanate AS, Majhail N, DeFilipp Z, et al. Updated Indications for Immune Effector Cell Therapy: 2023 Guidelines from the American Society for Transplantation and Cellular Therapy. *Transplant Cell Ther.* 2023;29(10):594-597. doi:10.1016/j.jtct.2023.07.002
2. KYMRIA® (tisagenlecleucel). Package insert. Novartis. U.S. Food and Drug Administration. June 2025. <https://www.fda.gov/media/107296/download>
3. YESCARTA® (axicabtagene ciloleucel). Package insert. Kite Pharma, Inc. U.S. Food and Drug Administration. February 2026. <https://www.fda.gov/media/108377/download>
4. TECARTUS® (brexucabtagene autoleucel). Package insert. Kite Pharma, Inc. U.S. Food and Drug Administration. April 2026. <https://www.fda.gov/media/140409/download>
5. BREYANZI® (lisocabtagene maraleucel). Package insert. Juno Therapeutics, Inc., a Bristol-Myers Squibb Company. U.S. Food and Drug Administration. February 2026. <https://www.fda.gov/media/145711/download>
6. ABECMA® (idecabtagene vicleucel). Package insert. Celgene Corporation, a Bristol-Myers Squibb Company. U.S. Food and Drug Administration. November 2025. <https://www.fda.gov/media/147055/download>
7. CARVYKTI® (ciltacabtagene autoleucel). Package insert. Janssen Biotech, Inc. U.S. Food and Drug Administration. October 2025. <https://www.fda.gov/media/156560/download>
8. AUCATZYL® (obecabtagene autoleucel). Package insert. Autolus Limited. U.S. Food and Drug Administration. February 2026. <https://www.fda.gov/media/183463/download>