CLINICAL POLICY AND PROCEDURE MANUAL

Policy Number: PA.216.CC
Last Review Date: 08/15/2024
Effective Date: 09/01/2024

PA.216.CC Car-T Therapy Policy

Summary
Cancer immunotherapy is treatment that uses a patient's immune system to attack tumors. One type of cancer immunotherapy is Chimeric antigen receptor (CAR) T-cell therapy. This therapy takes T-cells from a patient's blood, then using a disarmed virus, the T cells are genetically engineered to produce receptors on their surface called chimeric antigen receptors, or CARs. These special receptors allow the T cells to recognize and attach to a specific protein, or antigen, on tumor cells. The final step is the infusion of the CAR T cells into the patient (which is preceded by a "lymphodepleting" chemotherapy regimen). The CAR T cells recognize and kill cancer cells that harbor the antigen on their surfaces.

Side Effects
Like all cancer treatments, CAR-T Cell Therapy has potential side effects, which are sometimes fatal. One of the most common side effects of CAR-T Cell Therapy is Cytokine Release Syndrome (CRS). CRS can result in severe nausea, high fevers and large drops in blood pressure due to the massive release of cytokines into the bloodstream; this side effect can be managed with standard therapies to treat inflammatory conditions, including steroids.

Another potential side effect of CAR T-Cell Therapy is a mass die off of B cells, known a B-cell aplasia. Patients with B-cell aplasia must receive immunoglobulin therapy, which provides with the necessary antibodies to fight off infections.

There is the potential for neurotoxicity, from cerebral edema to confusion or seizure-like activity. Other serious side effects include allergic reactions during the infusion, electrolyte abnormalities and low blood cell counts.

This policy includes:

- Tisagenlecleucel (Kymriah)
- Axicabtagene Ciloleucel (Yescarta)
- Brexucabtagene Autoleucel (Tecartus)
- Lisocabtagene maraleucel (Breyanzi)
- Idecabtagene vicleucel (Abecma)
- Ciltacabtagene autoleucel (Carvykti)

Tisagenlecleucel (Kymriah)
KYMRIAH is a CD19-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of:

1. Pediatric and young adult patients (up to 25 years of age) with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.
    a. Member has experienced disease relapse after allogeneic stem cell transplantation (SCT) and member is ≥ 6 months from above transplantation at the time of infusion; OR
    b. Member has 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
    c. Member has relapsed/refractory Philadelphia chromosome-positive B-ALL that has progressed after failure of 2 prior regimens, including a Tyrosine Kinase Inhibitor (TKI)-containing regimen.
2. Adult patients 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.
    a. Members must have previously received at least two lines of therapy, including rituximab and an anthracycline (for DBCL) AND
    b. Either having failed autologous Hematopoietic stem cell transplantation (ASCT) or being ineligible for or not consenting to ASCT.

- Member must present CD19 tumor expression.
- Member must not have received prior CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
- Delay tisagenlecleucel infusion if patient 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.
- Tisagenlecleucel is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the KYMRIAH REMS. Information is available at www.kymriah-rems.com or 1-844-4KYMRIAH.

Axicabtagene Ciloleucel (Yescarta)

YESCARTA is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of:

1. Adult patients (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 stem-cell transplantation (ASCT); 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.
2. Adult patients with relapsed or refractory follicular lymphoma (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 (e.g. bendamustine, cyclosphamide) containing

regimen; or disease progression or relapse less ≤12 months after autologous stem-cell transplantation (ASCT). 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).

- Member must present CD19 tumor expression.
- Member must not have received prior CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
- Member must not have evidence of active infection or inflammatory disorders
- Axicabtagene ciloleucel (Yescarta) is only available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA and TECARTUS REMS. Contact Yescarta REMS at www.YescartaTecartusREMS.com or 1-844-454-5483.

Brexucabtagene Autoleucel (Tecartus)
TECARTUS is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of:

1. Adult patients (18 years of age and above) with relapsed or refractory mantle cell lymphoma (MCL).

   The Member's previous treatments must have included, but are not limited to, all of the following:
   a. Anthracycline or bendamustine-containing chemotherapy; and
   b. Anti-CD20 monoclonal antibody therapy (e.g. rituximab); and
   c. Bruton's tyrosine kinase inhibitor (BTKi) therapy (e.g. ibrutinib, acalabrutinib, zanubrutinib)

2. Adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

- Member must present CD19 tumor expression.
- Member must not have received prior CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
- Member must not have evidence of active infection or inflammatory disorders
- Brexucabtagene autoleucel is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA and TECARTUS REMS Program. Information is available at www.YescartaTecartusREMS.com or 1-844-454-KITE (5483)

Lisocabtagene maraleucel (Breyanzi)
BREYANZI 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

(including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B.

- Delay lisocabtagene maraleucel infusion if patient has unresolved serious adverse reaction from preceding chemotherapies, active uncontrolled infection, or active graft versus host disease (GVHD).
- Member must present CD19 tumor expression.
- Member must not have received prior CD19-directed chimeric antigen receptor (CAR) T-cell therapy.
- Lisocabtagene maraleucel (Breyanzi(R)) is only available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the BREYANZI REMS. Contact BREYANZI REMS at www.BreyanziREMS.com or 1-888-423-5436.

Idecabtagene vicleucel (Abecma)
ABECMA is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four 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 patient has unresolved serious adverse events (especially pulmonary events, cardiac events, or hypotension), including those after preceding chemotherapies or if patient has active infections or inflammatory disorders.
- Member must not have received prior chimeric antigen receptor (CAR) T-cell therapy.
- Idecabtagene vicleucel is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the ABECMA REMS. Contact ABECMA REMS at www.AbecmaREMS.com or contact Bristol-Myers Squibb at 1-888-423-5436.

Ciltacabtagene autoleucel (Carvykti)
CARVYKTI is a B-cell maturation antigen (BCMA)-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent, and an anti-CD38 monoclonal antibody.

Limitations
1. KYMRIAH is not indicated for treatment of patients with primary central nervous system lymphoma.
2. YESCARTA is not indicated for the treatment of patients with primary central nervous system lymphoma.
3. TECARTUS is not indicated for the treatment of patients with primary central nervous system lymphoma.
4. BREYANZI is not indicated for the treatment of patients with primary central nervous system lymphoma.

5. Car-T Therapy is authorized once per lifetime.
6. The treating facility is certified under the Risk Evaluation and Mitigation Strategy (REMS) System program appropriate to requested CAR-T product.

Codes

CPT and HCPCS codes covered when the above indications are met	
Code	Description
0537T	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
0538T	Chimeric antigen receptor T-cell (CAR-T) therapy; preparation of blood-derived T lymphocytes for transportation (e.g., cryopreservation, storage)
0539T	Chimeric antigen receptor T-cell (CAR-T) therapy; receipt and preparation of CAR-T cells for administration
0540T	Chimeric antigen receptor T-cell (CAR-T) therapy; CAR-T cell administration, autologous
C9399	Unclassified drugs or biologicals Abecma (idecabtagene vicleucel) received FDA approval on March 26, 2021. CMS has not yet assigned a HCPCS Level II code to this product. Until that time, report this biological with C9399 Unclassified drugs or biologicals. This code is used to bill newly approved products prior to assignment of a specific HCPCS Level II code.
J3590	Unclassified biologics
J9999	Not otherwise classified, antineoplastic drugs
Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 car positive viable 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	Abecma® (idecabtagene vicleucel)
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
S2107	Adoptive immunotherapy i.e. development of specific antitumor reactivity (e.g., tumor-infiltrating lymphocyte therapy) per course of treatment

References

1. American Cancer Society, How Immunotherapy is Used to Treat Cancer. Last Revised: December 27, 2019. https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/what-is-immunotherapy.html
2. National Cancer Institute. CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. Updated: March 10, 2022. https://www.cancer.gov/about-cancer/treatment/research/car-t-cells.
3. Kymriah prescribing information. https://www.fda.gov/media/107296/download
4. Yescarta prescribing information. https://www.fda.gov/media/108377/download
5. Tecartus prescribing information. https://www.fda.gov/media/140409/download
6. Breyanzi prescribing information. https://www.fda.gov/media/145711/download
7. Abecma prescribing information. https://www.fda.gov/media/147055/download
8. Carvykty prescribing information. https://www.fda.gov/media/156560/download
9. Decision Memo for Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers (CAG-00451N). August 7, 2019. https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=291
10. DiGrande, Samantha. NCCN Report on CAR T-Cell Therapy, Recommendations for Future Use. September 14, 2018. https://www.ajmc.com/view/nccn-report-on-car-tcell-therapy-recommendations-for-future-use
11. Schuster SJ, et al. JULIET Investigators. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019 Jan 3;380(1):45-56. https://www.nejm.org/doi/full/10.1056/nejmoa1804980

12. Maude SL, et al. Chimeric antigen receptor T cells for sustained remissions in leukemia. N Engl J Med. 2014 Oct 16;371(16):1507-17. https://www.nejm.org/doi/full/10.1056/nejmoa1407222
13. Neelapu et al, ZUMA-1 trial, N Engl J Med 2017; 377:2531-2544. DOI: 10.1056/NEJMoa1707447. Published: December 28, 2017. https://www.nejm.org/doi/full/10.1056/nejmoa1707447
14. Wang et al, Zuma-2 trial, N Engl J Med 2020; 382:1331-1342. DOI: 10.1056/NEJMoa1914347. Published: April 1, 2020. https://www.nejm.org/doi/10.1056/NEJMoa1914347

Revision History

Revision	Date
Policy Created	July, 2021
Approved	October, 2021
Removed termed code C9076, added new codes C9081 & Q2054	October, 2021
Removed termed code C9081, added coded C9399 and Q2055, formatting updates throughout policy, added items #2 under “Brexucabtagene Autoleucel (Tecartus)”, added links to References 10 through 14	December, 2021
Updated Logo	April, 2022
Added info related to new code C9098 Ciltacabtagene autoleucel	August, 2022
Removed termed temporary code C9098 and added replacement permanent code Q2056	October, 2022
Q4 2023 Review; updated Evolent Logo, changed Evolent Health to Evolent; formating updates to body of policy; deleted Last Accessed date and added Last Revised Date to Reference #1; deleted Last Accessed Date and added Updated Date to Reference #2; format updates to Reference #s 3, 4, 5, 6, 7, 8, 9, 10, 11 and 13	November, 2023
Q3 2024 Annual Review; minor format update to Reference #9; added Published Dates to Reference #s 13 and 14; removed invalid Reference #15 as no replacement was found.	August 15, 2024

Disclaimer

CountyCare medical payment and prior authorization policies do not constitute medical advice and are not intended to govern or otherwise influence the practice of medicine. The policies constitute only the reimbursement and coverage guidelines of County Care and its affiliated managed care entities. Coverage for services varies for individual members in accordance with the terms and conditions of applicable Certificates of Coverage, Summary Plan Descriptions, or contracts with governing regulatory agencies.

CountyCare reserves the right to review and update the medical payment and prior authorization guidelines in its sole discretion. Notice of such changes, if necessary, shall be provided in accordance with the terms and conditions of provider agreements and any applicable laws or regulations.