Medical Necessity Guidelines: Modified T-Cell Therapies

Effective: January 20, 2021

Prior Authorization Required If REQUIRED, submit supporting clinical documentation pertinent to service request.	**Yes ☒ No ☐**

Applies to:

COMMERCIAL Products

☒ Tufts Health Plan Commercial products; Fax: 617.972.9409

☒ Tufts Health Freedom Plan products; Fax: 617.972.9409

- CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

TUFTS HEALTH PUBLIC PLANS Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax:888.415.9055

☒ Tufts Health Together – MassHealth MCO Plan and Accountable Care Partnership Plans; Fax: 888.415.9055

☒ Tufts Health RITogether – A Rhode Island Medicaid Plan; Fax: 857.304.6404

☒ Tufts Health Unify* – OneCare Plan (a dual-eligible product); Fax: 857.304.6304

*The MNG applies to Tufts Health Unify members unless a less restrictive LCD or NCD exists.

SENIOR Products

- Tufts Health Plan Senior Care Options (SCO), (a dual-eligible product) – Refer to the Tufts Health Plan SCO Prior Authorization List
- Tufts Medicare Preferred HMO, (a Medicare Advantage product) – Refer to the Tufts Medicare Preferred HMO Prior Authorization and Inpatient Notification List

Note: In the absence of specific LCD/NCD guidance for CAR-T therapy, the above guidelines will also apply to **Tufts Medicare Preferred HMO** as they reflect the FDA-approved guidelines for these products.

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to make sure that prior authorization has been obtained.

OVERVIEW

Chimeric antigen receptor T-cell therapy (CAR-T cell therapy), a type of immunotherapy which may also be referred to as adoptive T-cell therapy, attempts to program patients' own immune systems to recognize and attack cancer cells. The first step in this therapy is to remove T-cells from the patient via apheresis, a process that removes blood from the body and removes one or more blood components (such as white blood cells, plasma, or platelets). The remaining blood is then returned to the body. The T-cells are then sent to a drug manufacturing facility or laboratory where they are genetically engineered to produce chimeric antigen receptors (CARs) on their surface. These CARs are what allow the T-cells to recognize an antigen on targeted tumor cells. The genetically modified T-cells are grown in the lab until there are enough of them (many millions) to freeze and return to the center treating the patient. There they are infused into the recipient with the expectation that the CAR T cells will recognize and kill cancerous cells that have the targeted antigen on their surface. Since the CAR-T cells may remain in the body long after the infusion, it is possible the treatment can bring about long-term remission.

Note: For **Tufts Health Together, Tufts Health Unify and Tufts Health Plan Senior Care Options** members:

- Refer to the MassHealth Drug List Table 75: Chimeric Antigen Receptor (CAR)-T Immunotherapies, Section III: Evaluation Criteria for Approval, to access prior authorization criteria for **Kymriah**, **Yescarta** and **Tecartus**

CLINICAL COVERAGE CRITERIA

There are currently three FDA-approved CAR-T cell therapy products, KYMRIAH™, YESCARTA™ and TECARTUS™. The guidelines for each are outlined below:

KYMRIAH™

Tufts Health Plan may authorize coverage of KYMRIAH (tisagenlecleucel) when **ONE** of the following is met:

1. The Member is age 25 years of age or younger, has been diagnosed with CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL), and has failed a minimum of two lines of treatment;
2. The Member is age 25 years of age or younger, has been diagnosed with B-cell precursor acute lymphoblastic leukemia (ALL), and is experiencing a second or later relapse[a] after a minimum of two lines of treatment;
3. The Member is age 18 years of age or older, has been diagnosed with CD19-positive 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, and has failed a minimum of two lines of systemic therapy;
4. The Member is age 18 years of age or older, has been diagnosed with 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, and is experiencing a biopsy proven relapse[b] after treatment with a minimum of two lines of systemic therapy;

   AND **ALL** of the following are met:

5. The Member has had no prior treatment with tisagenlecleucel or other gene therapy.
6. The Member does not have primary central nervous system (CNS) lymphoma.
7. The Member has adequate bone marrow, cardiac, pulmonary and organ function.
8. There is no active infection, including active hepatitis B or C.
9. For Members with a history of allogeneic stem cell transplantation, there is no indication of active graft vs. host disease.
10. The treating facility is certified under the KYMRIAH™ Risk Evaluation and Mitigation Strategy (REMS) System program. More information is available at us.kymriah.com/acute-lymphoblastic-leukemia-children/interested-in/where-to-get-treatment/.

[a] Relapse is defined as the reappearance of leukemic lymphoblasts in peripheral blood or bone marrow after there has been achievement of complete remission with other lines of treatment.

[b] Relapse is defined as biopsy proven return of DLBCL disease after achievement of complete remission with other lines of treatment.

YESCARTA™

Tufts Health Plan may authorize coverage of YESCARTA™ (axicabtagene ciloleucel) for the treatment of members age 18 and over when **ONE** of the following is met:

1. The Member has been diagnosed with CD19-positive 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, and DLBCL arising from follicular lymphoma, and has failed a minimum of two lines of systemic therapy;
2. The Member has been 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, and DLBCL arising from follicular lymphoma, and is experiencing a biopsy proven relapse[c] after treatment with a minimum of two lines of systemic therapy;

   AND **ALL** of the following are met:

3. The Member has had no prior treatment with axicabtagene ciloleucel or other gene therapy.
4. The Member does not have primary central nervous system (CNS) lymphoma.
5. The Member has adequate bone marrow, cardiac, pulmonary and organ function.
6. For Members with a history of allogeneic stem cell transplantation, there is no indication of active graft vs host disease.
7. There is no active infection, including active hepatitis B or C.
8. The treating facility is certified under the YESCARTA™ and TECARTUS™Risk Evaluation and Mitigation Strategy (REMS) System program. More information is available at yescartatecartusrems.com/

[c]Relapse is defined as biopsy proven return of DLBCL disease after achievement of complete remission with other lines of treatment.

TECARTUS™

Tufts Health Plan may authorize coverage of TECARTUS (brexucabtagene autoleucel) for the treatment of members age 18 or over when **ALL** of the following are met:

1. The Member has been diagnosed with relapsed or refractory mantle cell lymphoma (MCL), defined as disease progression after last treatment regimen or refractory to the most recent therapy, as confirmed by circulating clonal lymphocytes, bone marrow involvement and/or measurable lymphadenopathy.
2. The Member's previous treatments must have included, but are not limited to, **all** of the following:
   a. Anthracycline or bendamustine-containing chemotherapy
   b. Anti-CD20 monoclonal antibody therapy (e.g. rituximab)
   c. Bruton's tyrosine kinase inhibitor (BTKi) therapy (e.g. ibrutinib, acalabrutinib, zanubrutinib).
3. The Member has no active infection (e.g. viral, bacterial, fungal) including HIV, active hepatitis B or active hepatitis C. Screening must be completed at time of leukapheresis.
4. The Member has adequate bone marrow, cardiac, pulmonary, renal, and organ function.
5. For Member who has undergone a prior allogenic stem cell transplantation, there is no indication of active graft vs host disease (GVHD).
6. The Member has had no prior treatment with brexucabtagene autoleucel.
7. The Member has no detectable cerebrospinal fluid malignant cells or brain metastases, and no history of central nervous system (CNS) lymphoma.
8. The treating facility is certified under the YESCARTA™ and TECARTUS™Risk Evaluation and Mitigation Strategy (REMS) System program. More information is available at yescartatecartusrems.com.

LIMITATIONS

- CAR-T cell therapy is contraindicated in pregnancy.
- Members receiving immunosuppressive therapy for an autoimmune disorder will not be approved for CAR-T cell therapy.
- Members with untreated underlying primary immunodeficiency syndromes will not be approved for CAR-T cell therapy.
- Members with active and/or metastatic malignancy that is unlikely to respond to treatment will not be approve for CAR-T therapy.
- Members who have had prior treatment with any form of CAR-T cell therapy, including therapies in clinical trial settings, will not be approved for additional CAR-T therapy.
- CAR-T therapy will not be covered if the Member demonstrates clinical decompensation from time of authorization to time of infusion and no longer meets clinical coverage criteria.

Any indications for CAR-T cell therapy other than those outlined above are considered investigational and will not be covered.

CODES

The following codes require prior authorization:

Table 1: CPT Codes

CPT 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 (eg, 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

Table 2: HCPCS Codes

HCPCS Code	Description
Q2041	Axicabtagene Ciloleucel, up to 200 million autologous Anti-CD19 CAR T Cells, Including leukapheresis and dose preparation procedures, per infusion
Q2042	Tisagenlecleucel, up to 600 million CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
C9073	Brexucabtagene autoleucel, up to 200 million autologous anti-cd19 car positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose

REFERENCES

1. Hayes, Inc. Medical Technology Directory Report. Adoptive Immunotherapy Using Genetically Modified Lymphocytes for Lymphoproliferative Disorders and Hematological Malignancies. September 7, 2017. Available at hayesinc.com. Last accessed October 26, 2017.
2. United States Food and Drug Administration. Package Insert-KYMRIAH. Available at fda.gov. Last accessed May 3, 2018.
3. United States Food and Drug Administration. Package Insert-YESCARTA. Available at fda.gov. Last accessed October 26, 2017.
4. United States Department of Health and Human Services, National Institutes of Health, National Cancer Institute. CAR-T Cells: Engineering Patients' Immune Cells to Treat Their Cancers. Available at cancer.gov. Last accessed October 24, 2017.
5. Leukemia & Lymphoma Society. Chimeric Antigen Receptor (CAR) T-Cell Therapy Facts. Available at lls.org. Last accessed October 20, 2017.
6. Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. *N Engl J Med*. 2020;382(14):1331-1342. doi:10.1056/NEJMoa1914347.
7. Initial treatment of mantle cell lymphoma. UpToDate.com/login [via subscription only]. Accessed: July 30, 2020.
8. United States Food and Drug Administration. Package Insert-TECARTUS. Available at fda.gov. Last accessed August 18, 2020.
9. MassHealth Drug List Table 75: Chimeric Antigen Receptor (CAR)-T Immunotherapies accessed November 11, 2020 at masshealthdruglist.ehs.state.ma.us/MHDL/pubtheradetail.do?id=353
10. MassHealth Managed Care Entity Bulletin 42: Updated MassHealth Acute Hospital Carve-Out Drugs Requirements. Last accessed January 13, 2021 at mass.gov/doc/managed-care-entity-bulletin-42-updated-masshealth-acute-hospital-carve-out-drugs-requirements/download

APPROVAL HISTORY

February 14, 2018: Reviewed by the Integrated Medical Policy Advisory Committee (IMPAC), for effective date of May 12, 2018.

Subsequent endorsement date(s) and changes made:

- July 25, 2018: Reviewed by IMPAC, update to criteria section for Kymriah; update to age criteria for Yescarta; coding update.
- October 10, 2018: Reviewed by IMPAC, renewed without changes.
- October 2018: Template and disclaimer updated.
- January 1, 2019: AMA CPT® coding update, effective January 1, 2019, the following CPT codes added to Table 1: 0537T, 0538T, 0539T, 0540T; the following HCPCS code added to Table 2 (formerly Table 1): Q2042; the following HCPCS code removed from Table 2(code deleted) : Q2040.
- October 16, 2019: Reviewed by IMPAC, renewed without changes.
- September 16, 2020: Reviewed at IMPAC. Addition of criteria for Tecartus.
- October 21, 2020: Reviewed by IMPAC, renewed without changes
- November 4, 2020: Fax number for Unify updated
- November 18, 2020: Reviewed at IMPAC. For effective date November 18, 2020, removed noncoverage of Tecartus when member is with history of CNS disorders criterion. MassHealth Table 75: Chimeric Antigen Receptor (CAR)-T Immunotherapies: Evaluation criteria for approval of Kymriah and Yescarta is applicable criteria for prior authorization review for Tufts Health Together per MassHealth Managed Care Entity Bulletin 42

- December 16, 2020: Reviewed at IMPAC. MassHealth Table 75: Chimeric Antigen Receptor (CAR)-T Immunotherapies: Evaluation criteria for approval of Kymriah and Yescarta is applicable criteria for prior authorization review for Tufts Health Unify and Tufts Health Plan Senior Care Options
- January 1, 2021: Coding update, effective January 1, 2021, the following HCPCS code added to Table 2: C9073; the following HCPCS code removed from Table 2: J9999.
- January 20, 2021: Reviewed at IMPAC. MassHealth Table 75: Chimeric Antigen Receptor (CAR)-T Immunotherapies: Evaluation criteria for approval of Tecartus is applicable criteria for prior authorization review for Tufts Health Together, Tufts Health Unify and Tufts Health Plan Senior Care Options.

BACKGROUND, PRODUCT AND DISCLAIMER INFORMATION

Medical Necessity Guidelines are developed to determine coverage for benefits, and are published to provide a better understanding of the basis upon which coverage decisions are made. We make coverage decisions using these guidelines, along with the Member's benefit document, and in coordination with the Member's physician(s) on a case-by-case basis considering the individual Member's health care needs.

Medical Necessity Guidelines are developed for selected therapeutic or diagnostic services found to be safe and proven effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in our service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. We revise and update Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of Members. The use of this guideline is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to eligibility and benefits on the date of service, coordination of benefits, referral/authorization, utilization management guidelines when applicable, and adherence to plan policies, plan procedures, and claims editing logic.