Tecartus (brexucabtagene autoleucel)
Clinical Coverage Criteria

Overview

Chimeric antigen receptor (CAR) T-cell therapies are immunotherapies that target specific types of cancer. CAR T-cell therapies are made are made by collecting T-cells from the patient and re-engineering them in the laboratory to produce proteins on their surface called chimeric antigen receptors, or CARs. The CARs recognize and bind to specific proteins, or antigens, on the surface of cancer cells and kill them. Since 2017, six CAR T-cell therapies have been approved by the Food and Drug Administration (FDA). All are approved for the treatment of blood cancers, including lymphomas, some forms of leukemia, and, most recently, multiple myeloma. The CAR T-cell therapies approved by FDA to date target one of two antigens on B-cells, CD19 or BCMA.

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

- Adult patients with relapsed or refractory mantle cell lymphoma (MCL).
  This indication is approved under accelerated approval based on overall response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

Full prescribing information available at: https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/tecartus. The Tecartus (brexucabtagene autoleucel) label has a boxed warning:

WARNING: CYTOKINE RELEASE SYNDROME, NEUROLOGICAL TOXICITIES, and SECONDARY HEMATOLOGICAL MALIGNANCIES

See full prescribing information for the complete boxed warning.

- Cytokine release syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving TECARTUS. Do not administer TECARTUS to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids
- Neurological toxicities, which may be severe or life-threatening, can occur following treatment with TECARTUS, including concurrently with CRS. Monitor for neurological events after treatment with TECARTUS. Provide supportive care as needed.
- T cell malignancies have occurred following treatment of hematological malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including TECARTUS.
- TECARTUS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the TECARTUS REMS.

Despite the therapeutic successes of CAR T-cell therapy, the intervention carries the risk of severe side effects. These include cytokine release syndrome (CRS), neurologic toxicities and B-cell aplasia, all of which can be life-threatening. On August 30, 2017, tocilizumab (Actemra) was FDA-approved to treat CAR T-cell induced CRS in in adults and in pediatric patients 2 years of age and older.

Because of the risk of CRS and neurological toxicities, Tecartus is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Tecartus REMS. The required components of the Tecartus REMS are:

- Healthcare facilities that dispense and administer Tecartus must be enrolled and comply with the REMS requirements.
- Certified healthcare facilities must have on-site, immediate access to tocilizumab, and ensure that a minimum of two doses of tocilizumab are available for each patient for administration within 2 hours after Tecartus infusion, if needed for treatment of CRS.
- Certified health care facilities must ensure that health care providers who prescribe, dispense, or administer Tecartus are trained in the management of CRS and neurological toxicities

Tecartus (brexucabtagene autoleucel) is only available at select treatment centers. Further information is available at: https://www.yescartatecartusrems.com/.

Policy

This Policy applies to the following Fallon Health products:

☒ Fallon Medicare Plus, Fallon Medicare Plus Central (Medicare Advantage)
☒ MassHealth ACO
☒ NaviCare HMO SNP (Dual Eligible Medicare Advantage and MassHealth)
☒ NaviCare SCO (MassHealth-only)
☒ PACE (Summit Eldercare PACE, Fallon Health Weinberg PACE)
☒ Community Care (Commercial/Exchange)

Prior authorization by a Fallon Health Medical Director is required for Tecartus (brexucabtagene autoleucel). This prior authorization is separate from any prior authorization that may be required for the member's inpatient or outpatient encounter. Medical records from the providers who have diagnosed or treated the symptoms prompting this request are also required.

Medicare Advantage (Fallon Medicare Plus, Fallon Medicare Plus Central)
Fallon Health complies with CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations for Medicare Advantage members. When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health may create internal coverage criteria under specific circumstances described at § 422.101(b)(6)(i) and (ii).

Medicare statutes and regulations do not have coverage criteria for Chimeric Antigen Receptor (CAR) T-cell therapy. Medicare has an NCD for Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24), Version Number 1, Effective Date of this Version: 08/07/2019 (Medicare Coverage Database Search 05/27/2024).

Coverage criteria for CAR T-cell therapy are fully established by Medicare, therefore, the Plan's coverage criteria are not applicable.

Link: **NCD Chimeric Antigen Receptor (CAR) T-cell Therapy (110.24)**

B. Nationally Covered Indications
Effective for services performed on or after August 7, 2019, Medicare covers autologous treatment for cancer with T-cells expressing at least one chimeric antigen receptor (CAR) when administered at healthcare facilities enrolled in the FDA risk evaluation and mitigation strategies (REMS) and used for a medically accepted indication as defined at Social Security Act section 1861(t)(2), i.e., is used for either an FDA-approved indication (according to the

FDA-approved label for that product), or for other uses when the product has been FDA-approved and the use is supported in one or more CMS-approved compendia.

C. Nationally Non-Covered
Effective for services performed on or after August 7, 2019, the use of non-FDA-approved autologous T-cells expressing at least one CAR is non-covered. Autologous treatment for cancer with T-cells expressing at least one CAR is non-covered when the requirements in Section A are not met.

D. Other
Effective for services performed on or after August 7, 2019, routine costs in clinical trials that use CAR T-cell therapy as an investigational agent that meet the requirements listed in NCD 310.1 will be covered.

MassHealth ACO
Fallon Health follows Medical Necessity Guidelines published by MassHealth when making medical necessity determinations for MassHealth members. In the absence of Medical Necessity Guidelines published by MassHealth, Fallon Health may create clinical coverage criteria in accordance with the definition of Medical Necessity in 130 CMR 450.204.

The MassHealth Drug List has medical necessity criteria for Kymriah (tisagenlecleucel) (MassHealth website search 05/27/2024), therefore, the Plan's coverage criteria are not applicable.

Link: **Tecartus (brexucabtagene autoleucel)**

NaviCare HMO SNP, NaviCare SCO
For plan members enrolled in NaviCare, Fallon Health first follow's CMS's national coverage determinations (NCDs), local coverage determinations (LCDs) of Medicare Contractors with jurisdiction for claims in the Plan's service area, and applicable Medicare statutes and regulations when making medical necessity determinations.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, or if the NaviCare member does not meet coverage criteria in applicable Medicare statutes, regulations, NCDs or LCDs, Fallon Health then follows Medical Necessity Guidelines published by MassHealth when making necessity determinations for NaviCare members.

PACE (Summit Eldercare PACE, Fallon Health Weinberg PACE)
Each PACE plan member is assigned to an Interdisciplinary Team. PACE provides participants with all the care and services covered by Medicare and Medicaid, as authorized by the interdisciplinary team, as well as additional medically necessary care and services not covered by Medicare and Medicaid. With the exception of emergency care and out-of-area urgently needed care, all care and services provided to PACE plan members must be authorized by the interdisciplinary team.

Fallon Health Clinical Coverage Criteria

Fallon Health Clinical Coverage Criteria for Tecartus (brexucabtagene autoleucel) apply to Community Care members. For Medicare Advantage, MassHealth ACO, NaviCare and PACE plan members, follow the applicable criteria described in the Policy section above.

Relapsed or Refractory Mantle Cell Lymphoma
A single administration of Tecartus (brexucabtagene autoleucel) may be considered medically necessary when all of the following criteria are met:
1. The member is ≥ 18 years of age at the time of informed consent.

2. The member has mantle cell lymphoma (MCL) that is pathologically confirmed MCL, with documentation of either overexpression of cyclin D1 or presence of t(11;14).
3. At least 1 measurable lesion according to the revised IWG Response Criteria for Malignant Lymphoma (Cheson et al. 2007).
4. Relapsed or refractory disease, defined by the following:
    - Disease progression after last regimen, or
    - Refractory disease is defined as failure to achieve partial response or complete response to the last regimen.
5. Up to 5 prior regimens for MCL. Prior therapy must have included:
    - Anthracycline or bendamustine-containing chemotherapy, and
    - Anti-CD20 monoclonal antibody therapy, and
    - Ibrutinib or acalabrutinib.
6. Treatment will be administered at a healthcare facility that is enrolled in the FDA Risk Evaluation and mitigation strategies (REMS) for Tecartus.

Induction plus consolidation/maintenance and/or all treatments occurring between sequential complete responses was counted as 1 regimen.

Relapsed or Refractory B-cell precursor Acute Lymphoblastic Leukemia
A single administration of Tecartus (brexucabtagene autoleucel) may be considered medically necessary when all of the following criteria are met:
7. The member is ≥ 18 years of age at the time of informed consent.
8. The member has relapsed or refractory B-precursor acute lymphoblastic leukemia (ALL), defined as one of the following:
    a. Primary refractory disease
    b. First relapse if first remission ≤ 12 months
    c. Relapsed or refractory disease after two or more lines of systemic therapy
    d. Relapsed or refractory disease after allogeneic transplant provided subject is at least 100 days from stem cell transplant at the time of enrollment and off of immunosuppressive medications for at least 4 weeks prior to enrollment
9. Subjects with Philadelphia chromosome positive (Ph+) disease are eligible if they are intolerant to tyrosine kinase inhibitor (TKI) therapy, or if they have relapsed/refractory disease despite treatment with at least 2 different TKIs
10. Treatment will be administered at a healthcare facility that is enrolled in the FDA Risk Evaluation and mitigation strategies (REMS) for Tecartus.

Exclusions

- Prior treatment with any CAR T-cell therapy.
- All other indications for Tecartus (brexucabtagene autoleucel) are considered experimental/investigational and not medically necessary.

Summary of Evidence

Relapsed or Refractory Mantle Cell Lymphoma

Mantle-cell lymphoma is a B-cell non-Hodgkin's lymphoma that generally has an aggressive clinical course. Bruton's tyrosine kinase (BTK) inhibitors have greatly improved outcomes in patients with relapsed or refractory mantle-cell lymphoma, yet patients who have disease progression after the receipt of BTK inhibitor therapy have a very poor prognosis, with an objective response occurring in 25 to 42% of patients and a median overall survival of 6 to 10 months with salvage therapies. Although allogeneic stem-cell transplantation is an option for some patients with relapsed or refractory mantle-cell lymphoma, non–relapse-related mortality, even with reduced-intensity conditioning therapy, remains high at 10 to 24% (Wang et al., 2020).

U.S. Food & Drug Administration (FDA) Pivotal Trial
ZUMA-2 (NCT02601313) is a single-arm, open-label, multicenter trial evaluated the efficacy and safety of a single infusion of Tecartus in adult patients (≥18 years of age) had histologically

confirmed mantle cell lymphoma (MCL) with either cyclin D1 overexpression or presence of the translocation t(11;14) and had disease that was either relapsed or refractory to up to five previous regimens for mantle-cell lymphoma. Previous therapy must have included anthracycline- or bendamustine-containing chemotherapy, an anti-CD20 antibody, and BTK inhibitor therapy with ibrutinib or acalabrutinib. BTK inhibitor therapy was not required to be the last line of therapy before trial entry, and patients were not required to have disease that was refractory to BTK inhibitor therapy. Eligible patients had disease progression after their last regimen or refractory disease to their most recent therapy. ZUMA-2 excluded patients with active or serious infections, prior allogeneic hematopoietic stem cell transplant, detectable cerebrospinal fluid malignant cells or brain metastases, and any history of central nervous system (CNS) lymphoma or CNS disorders.

Results of ZUMA-2 are published by Wang et al., 2020. The primary end point was the percentage of patients with an objective response (complete or partial response) as assessed by the independent radiology review committee according to the Lugano classification. Bone marrow evaluation in addition to PET-CT was necessary to confirm a complete response. Secondary end points included the duration of response, progression-free survival, overall survival, the percentage of patients with an investigator-assessed objective response according to the criteria of Cheson et al., 2007[1] the incidence of adverse events, the levels of CAR T cells in blood and cytokines in serum, and changes in scores from baseline to month 6 in the five-level version of the European Quality of Life–5 Dimensions (EQ-5D) questionnaire.

From October 24, 2016, to April 16, 2019, a total of 74 patients were enrolled in the trial and underwent leukapheresis. Tecartus was successfully manufactured for 71 patients (96%) and administered to 68 (92%). The median time from leukapheresis to the delivery of Tecartus at the trial site was 16 days. A total of 3 patients for whom the manufacturing of Tecartus failed did not proceed to an additional apheresis owing to deep-vein thrombosis, death from progressive disease, or withdrawal of consent (in 1 patient each). Two patients who had successful manufacture of KTE-X19 died from progressive disease before the receipt of conditioning chemotherapy. After the receipt of conditioning chemotherapy, 1 patient with ongoing atrial fibrillation, an exclusion criterion, was deemed to be ineligible for Tecartus infusion. As of July 24, 2019, the median follow-up among the patients in the primary efficacy analysis was 12.3 months (range, 7.0 to 32.3).

High-risk features were common at baseline, and most patients had received at least three previous lines of therapy. All the patients had disease that was refractory to BTK inhibitor therapy or had disease that had progressed during or after receipt of a BTK inhibitor. A total of 42 of 68 treated patients (62%) had disease that did not respond to BTK inhibitor therapy (primary refractory disease), and 18 (26%) had a relapse after having an initial response while receiving BTK inhibitor therapy; therefore, 88% of the treated patients had disease that was considered to be refractory to BTK inhibitor therapy. A total of 5 patients (7%) had a relapse after stopping BTK inhibitor therapy; 3 patients (4%) were unable to take ibrutinib owing to adverse events.

Among the first 60 treated patients who had at least 7 months of follow-up (as specified in the protocol), 93% (95% confidence interval [CI], 84 to 98) had an objective response as assessed by the independent radiologic review committee, with 67% (95% CI, 53 to 78) having a complete response. High concordance (95%) was observed between rates assessed by the independent radiologic review committee and those assessed by the investigator. Among all 74 enrolled patients, 85% had an objective response, with 59% having a complete response. The percentages of patients with an objective response were consistent among key subgroups, including patients with high-risk features. The median time to an initial response was 1.0 month (range, 0.8 to 3.1), and the median time to a complete response was 3.0 months (range, 0.9 to 9.3). Among the 42 patients who initially had a partial response or stable disease, 24 patients

[1] Cheson BD, Pfistner B, Juweid ME, et al. Revised response criteria for malignant lymphoma. J Clin Oncol 2007; 25: 579-86.

(57%), including 21 with an initial partial response and 3 with stable disease, subsequently had a complete response after a median of 2.2 months (range, 1.8 to 8.3) after the initial response; 17 patients were continuing to have a response as of the data-cutoff date (median follow-up, 12.3 months).

Minimal residual disease was analyzed in 29 of 74 patients (39%); 24 of these 29 patients (83%) (19 patients with a complete response and 5 with a partial response) had no detectable residual disease (i.e., <1 in 100,000 cells) at week 4, and 15 of 19 patients (79%) with available data had negative results at month 6. Two patients who had disease progression after having an objective response to Tecartus received a second infusion approximately 1 year and 1.3 years after the initial infusion; analysis in these patients is ongoing.

A total of 57% of all the patients in the primary efficacy analysis and 78% of the patients who had a complete response were in remission as of the data-cutoff date. The first 28 patients who were treated had a median follow-up of 27.0 months (range, 25.3 to 32.3), with 43% having a continued remission without additional therapy. The percentages of patients with an ongoing response were also consistent across key covariates. The 3 patients who had CD19-negative tumors at baseline and were included in the primary efficacy analysis had a complete response and were in remission as of the data-cutoff date.

At 12 months, the estimated progression-free survival and overall survival were 61% and 83%, respectively. Subgroup analysis showed that progression-free survival at 6 months was consistent among patients with poor prognostic features, including pleomorphic morphologic characteristics, *TP53* mutation, or a Ki-67 proliferation index of 50% or higher.

At the time of analysis, 76% of all 68 treated patients were alive. Among the patients who had a response, progressive disease developed in 14. One patient who had a partial response underwent allogeneic stem-cell transplantation.

All 68 treated patients had at least one adverse event of any grade, with adverse events of grade 3 or higher occurring in 99% of the patients. The most common adverse events of grade 3 or higher were cytopenias (in 94% of the patients) and infections (in 32%). Grade 3 or higher cytopenias included neutropenia (in 85% of patients), thrombocytopenia (51%), and anemia (50%).

The cytokine release syndrome occurred in 91% of the patients. No patient died from cytokine release syndrome. Most cases were grade 1 or 2 (in 76% of patients), with cases of grade 3 or higher occurring in 15% of the patients. For the management of cytokine release syndrome, 59% of all treated patients received tocilizumab, 22% received glucocorticoids, and 16% received vasopressors. The median time after infusion to the onset of cytokine release syndrome of any grade was 2 days (range, 1 to 13); the corresponding interval to the onset of cytokine release syndrome of grade 3 or higher was 4 days (range, 1 to 9). All events resolved within a median of 11 days.

A total of 63% of patients had neurologic events. No patient died from a neurologic event. Neurologic events of grade 1 or 2 occurred in 32% of the patients and events of grade 3 or higher in 31%. One patient had grade 4 cerebral edema and fully recovered with aggressive multimodality therapy including ventriculostomy. For the management of neurologic events, 26% of all treated patients received tocilizumab and 38% received glucocorticoids.

A total of 68% of patients had serious adverse events. Infection of grade 3 or higher occurred in 32% of the patients, with the most common being pneumonia (in 9%).

A total of 16 patients (24%) who received Tecartus died, primarily from progressive disease

(14 patients). Two patients had grade 5 adverse events, including organizing pneumonia related to conditioning chemotherapy in 1 patient and staphylococcus bacteremia related to conditioning chemotherapy and Tecartus therapy in 1 patient.

Relapsed or Refractory B-cell precursor Acute Lymphoblastic Leukemia

Acute lymphoblastic leukemia (ALL) is a heterogeneous hematologic disease characterized by the proliferation of immature lymphoid cells in the bone marrow, peripheral blood, and other organs (Jabbour et al., 2005). The age-adjusted incidence rate of ALL in the United States is 1.8 per 100,000 individuals per year, with approximately 6550 new cases and 1330 deaths estimated in 2024 (Howlader et al., 2021; Siegel et al., 2024). The median age at diagnosis for ALL is 17 years, with 53.5% of patients diagnosed at <20 years of age. In contrast, 29.6% of patients are diagnosed at ≥45 years of age and only approximately 13.7% of patients are diagnosed at ≥65 years of age (Howlader et al., 2021). ALL represents 75% to 80% of acute leukemias among children, making it the most common form of childhood leukemia; by contrast, ALL represents approximately 20% of all leukemias among adults Jabbour et al., 2005; Esparza et al., 2005).

The cure rates and survival outcomes for patients with ALL have improved dramatically over the past several decades, primarily among children. Improvements are largely owed to advances in the understanding of the molecular genetics and pathogenesis of the disease, the incorporation of minimal residual disease (MRD) testing, the refinement of risk-adapted treatment algorithms, the advent of new targeted agents, and the use of allogeneic hematopoietic cell transplantation (Ma et al., 2014).

U.S. Food & Drug Administration (FDA) Pivotal Trial
From Food and Drug Administration (FDA) Tecartus, Kite Pharmaceuticals, Inc. Package Insert (Revised: 04/2024)

The efficacy of Tecartus for the treatment of relapsed or refractory b-cell precursor acute lymphoblastic leukemia (ALL) was evaluated in ZUMA-3 (NCT02614066), an open-label, single-arm, multicenter trial. Results are published by Shah et al., 2021. Eligible patients were 18 years of age or older with Eastern Cooperative Oncology Group performance status of 0-1, and morphological disease in the bone marrow (>5% blasts), first relapse following a remission lasting ≤ 12 months, relapsed or refractory ALL after second-line or higher therapy, or relapsed or refractory ALL at least 100 days after allogeneic stem cell transplantation. The study excluded patients with active or serious infections, active graft-vs-host disease or taking immunosuppressive medications within 4 weeks prior to enrollment, and any history of CNS disorders, including CNS-2 disease with neurologic changes and CNS-3 disease irrespective of neurological changes.

The primary endpoint was the rate of overall complete remission or complete remission with incomplete haematological recovery by central assessment. Duration of remission and relapse-free survival, overall survival, minimal residual disease (MRD) negativity rate, and allogeneic stem cell transplant rate were assessed as secondary endpoints. Efficacy and safety analyses were done in the treated population (all patients who received a dose of Tecartus).

Treatment consisted of lymphodepleting chemotherapy (fludarabine 25 mg/m2 iv daily on Days -4, -3 and -2; cyclophosphamide 900 mg/m2 iv on Day -2) followed by a single intravenous infusion of Tecartus at a target dose of 1×10^6 anti-CD19 CAR T cells/kg (maximum 1×10^8 cells) on Day 0. All treated patients were hospitalized until at least Day 7.

Between Oct 1, 2018, and Oct 9, 2019, 71 patients were enrolled and underwent leukapheresis. Six of these patients did not receive Tecartus due to manufacturing failure, eight patients were not treated primarily due to adverse events following leukapheresis, two patients underwent leukapheresis and received lymphodepleting chemotherapy but were not treated with Tecartus, and one patient treated with Tecartus was inevaluable for efficacy. Among the remaining 54 efficacy-evaluable patients, the median time from leukapheresis to product delivery was 16 days

(range: 11 to 39 days) and the median time from leukapheresis to Tecartus infusion was 29 days (range: 20 to 60 days).

Of the 54 patients who were efficacy evaluable, the median age was 40 years (range: 19 to 84 years), 61% were male, and 67% were White, 6% were Asian, 2% were Black or African American, and 2% were American Indian or Alaska Native. At enrollment, 46% had refractory relapse, 26% had primary refractory disease, 20% had untreated second or later relapse, and 7% had first untreated relapse.

Among prior therapies, 43% of patients were previously treated with allogeneic stem cell transplantation, 46% with blinatumomab, and 22% with inotuzumab. Twenty-six percent of patients were Philadelphia chromosome positive (Ph+). Fifty (93%) patients had received bridging therapy between leukapheresis and lymphodepleting chemotherapy to control disease burden.

The efficacy of Tecartus was established on the basis of complete remission (CR) within 3 months after infusion and the duration of CR (DOCR). Twenty-eight (51.9%) of the 54 evaluable patients achieved CR, and with a median follow-up for responders of 7.1 months, the median DOCR was not reached. The median time to CR was 56 days (range: 25 to 86 days). All efficacy evaluable patients had potential follow-up for ≥ 10 months with a median actual follow-up time of 12.3 months (range: 0.3 to 22.1 months).

Efficacy Results in Adult Patients with Relapsed/Refractory B-cell precursor ALL

	Efficacy Evaluable Patients [a] N= 54	**All Leukapheresed Patients N = 71**
OCR rate (CR + CRi), n (%) [95% CI]	35 (64.8) [51, 77]	36 (50.7) [39, 63]
CR rate, n (%) [95% CI]	28 (51.9) [37.8, 65.7]	29 (40.9) [29.3, 53.2]
Duration of Remission, Median in months [95% CI] (Range [b] in months)	13.6 [9.4, NE] (0.03+, 16.07+)	13.6 [8.7, NE] (0.03+, 16.07+)
DOR, if best response is CR, median in months [95% CI] (Range in months)	NR [9.6, NE] (0.03+, 16.07+)	13.6 [9.4, NE] (0.03+, 16.07+)
DOR, if best response is CRi, median in months [95% CI] (Range in months)	8.7 [1.0, NE] (0.03+, 10.15+)	8.7 [1.0, NE] (0.03+, 10.15+)
Median Follow-up for CR in months	7.1 (0.03+, 16.1+)	5.0 (0.03+, 16.1+)

CI, confidence interval; CR, complete remission; CRi, complete remission with incomplete blood count recovery; DOR, duration of remission; NE, not estimable; NR, not reached, OCR, overall complete remission; NE, not estimable

[a] Of the 71 patients that were enrolled (and leukapheresed), 57 patients received lymphodepleting chemotherapy, and 55 patients
received TECARTUS. 54 patients were included in the efficacy-evaluable population.

[b] A + sign indicates a censored value.

Analysis of Evidence (Rational for Determination)

The development of CAR T-cell therapy has been a decades-long journey from when the technology was first proposed in the late 1980s to the U.S. Food and Drug Administration (FDA) approval of Novartis's tisagenlecleucel in 2017. Research to further optimize CAR T-cell design and delivery raises the hope of a cure for many more people with malignancies and heralds an exciting new era in cancer treatment. Data continue to accumulate supporting the efficacy of responses to anti-CD19 CAR-T cell therapy in B-cell malignancies.

Despite promising early response rates in trials, applying this data to real-world patients is challenging, partly as inclusion criteria favor better prognosis groups. Durability of remissions and incidence of long-term adverse events are critical factors determining the utility of anti-CD19 CAR T-cell therapy, but long-term follow-up of patients treated with anti-CD19 CAR T-cells is limited.

The majority of clinical trials using CAR-T cells are early phase studies. Randomized controlled clinical trials will better establish the place for CAR-T cells in relation to existing potentially curative therapies in B-cell malignancies. The selection of suitable patients for the application of CAR T-cells is important. The factors that drive the curative potential of CAR T-cell therapy may be fundamentally different than the factors that drive outcomes with autologous stem cell transplantation, which are predominantly related to chemotherapy sensitivity.

Coding

Medicare and Community Care members
Per CMS instructions (SE19009), when CAR T-cell therapies are administered in the inpatient setting, the hospital reports CAR T-Cell therapy using revenue code 0891 – Special Processed Drugs – FDA (U.S. Food and Drug Administration) Approved Cell Therapy – Charges for Modified Cell Therapy. Payment for the various steps required to collect and prepare CAR T-cell is included in payment for the CAR T-Cell.

Per CMS instructions (SE19009), when CAR T-cell therapies are administered in the hospital outpatient setting, outpatient hospitals should report CPT code 0540T with revenue code 0874 for the administration and HCPCS code Q2042 with revenue codes 0891 for the biological. Payment for the procedures described by CPT codes 0537T (collection/handling), 0538T (preparation for transport), and 0539T (receipt and preparation) represent the various steps required to collect and prepare the genetically modified T-cells, and these steps are not paid separately under the OPPS (under OPPS these codes, not separately paid, status indicator = B). Outpatient hospitals may report the charges for these various steps to collect and prepare the CAR T-cells separately to allow tracking of these services when furnished in the outpatient setting. However, the claim lines will reject as Medicare does not pay for these services under the OPPS.

In instances when CAR T-cell therapy is not ultimately administered to the member, but the preparation services are initiated or performed, the provider may not report the Q-code (which only applies when the T-cells are administered). Outpatient hospitals may report CPT codes 0537T, 0538T, and 0539T (as appropriate) and the charges associated with each code under the appropriate revenue code on the outpatient hospital claim. Medicare OPPS will reject these codes.

When the CAR T-cell preparation services occur in the hospital outpatient setting, but the administration of the CAR T-cells occurs in the inpatient setting, the outpatient hospital cannot report the drug Q code (which only applies when the T-cells are administered). Per CMS instructions (SE19009), inpatient hospitals may report the charges associated with the various steps for the collection and preparation of the CAR T-cells on the inpatient claim separately using revenue codes 0871, 0872, or 0873.

Alternatively, the hospital may include the charges for these various steps in the charge reported for the CAR T-Cell therapy using revenue code 0891 – Special Processed Drugs – FDA (U.S. Food and Drug Administration) Approved Cell Therapy – Charges for Modified Cell Therapy.

When the CAR T-cells are collected in the hospital outpatient setting and the CAR T-cell is administered in the hospital inpatient setting, inpatient providers should report the date that the CAR-T administration took place and not the date the cells were collected.

Source: MLN Matters®. Chimeric Antigen Receptor (CAR) T-Cell Therapy Revenue Code and HCPCS Setup Revisions SE19009. Article Release Date: March 17, 2022.

Procedure codes
The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

Use the following revenue codes for billing inpatient CAR T-cell therapy services:

Revenue Code	Revenue Code Description
0871	Cell/Gene Therapy – Cell Collection
0872	Cell/Gene Therapy – Specialized Biologic Processing and Storage - Prior to Transport
0873	Cell/Gene Therapy – Storage and Processing after Receipt of Cells from Manufacturer
0874	Cell/Gene Therapy – Infusion of Modified Cells
0891	Special Processed Drugs – FDA (U.S. Food and Drug Administration) Approved Cell Therapy – Charges for Modified cell therapy

Use the following revenue and CPT codes for billing outpatient CAR T-cell Services:

Revenue Code	Revenue Code Description	CPT/HCPCS Code	CPT/HCPCS Code Description
0871	Cell/Gene Therapy – Cell Collection	0537T	Chimeric antigen receptor t-cell (car-t) therapy; harvesting of blood-derived t lymphocytes for development of genetically modified autologous cart cells, per day
0872	Cell/Gene Therapy – Specialized Biologic Processing and Storage - Prior to Transport	0538T	Chimeric antigen receptor t-cell (car-t) therapy; preparation of blood-derived t lymphocytes for transportation (eg, cryopreservation, storage)
0873	Cell/Gene Therapy – Storage and Processing after Receipt of Cells from Manufacturer	0539T	Chimeric antigen receptor t-cell (car-t) therapy; receipt and preparation of car-t cells for administration
0874	Cell/Gene Therapy – Infusion of Modified Cells	0540T	Chimeric antigen receptor t-cell (car-t) therapy; car-t cell administration, autologous
0891	Special Processed Drugs – FDA (U.S. Food and Drug Administration) Approved Cell Therapy – Charges for Modified cell therapy	Q2043	Brexucabtagene autoleucel, up to 200 million autologous anti-cd19 car positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose

MassHealth ACO members
In accordance with MassHealth Managed Care Entity Bulletin 42, Fallon Health requires hospitals to take the following actions with respect to drugs and biologics (including CAR T-cell therapies) on the MassHealth Acute Hospital Carve-Out List for MassHealth ACO plan members:

1. Drugs and biologics on the MassHealth Acute Hospital Carve-Out Drugs List require prior authorization. The hospital must obtain prior authorization for the drug or biologic from Fallon Health or our designated pharmacy vendor. This prior authorization is separate from any prior authorization that may be required for the member's inpatient or outpatient encounter.
2. A drug or biologic designated by MassHealth as a carve-out drug must not be included on the facility/institutional claim that the hospital submits for the plan member's inpatient or outpatient encounter.
3. The hospital must instead submit a separate claim for the carve-out drug on a facility/institutional claim form (i.e., UB-04). (In other words, the drug is the only item on the

UB-04 claim.) The charge reported on the claim must be the "hospital's actual acquisition cost" for the drug.*

4. The claim for the carve-out drug must be reported with revenue code 0636 (Drugs requiring detailed coding), the HCPCS code for the drug, the National Drug Code (NDC) for the drug, and number of units administered.
5. The hospital must also include the following as separate attachments to the claim:
   a. A statement of the hospital's actual acquisition cost of the carve-out drug (as defined below) used to treat the member; and
   b. A copy of the invoice(s) for the carve-out drug from the drug manufacturer, supplier, distributor, or other similar party or agent; and
   c. Other additional documentation that the Plan deems necessary to evidence the hospital's actual acquisition cost of the carve-out drug.

* For purposes of this requirement, the "hospital's actual acquisition cost" of the carve-out drug is defined as follows:
"…*the hospital's invoice price for the drug, net of all on-or-off invoice reductions, discounts, rebates, charge backs and similar adjustments that the hospital has or will receive from the drug manufacturer or other party for the drug that was administered to the member including any efficacy, outcome, or performance-based guarantees (or similar arrangements), whether received pre-or post-payment*."

The MassHealth Acute Hospital Carve-out Drugs List is available at: https://masshealthdruglist.ehs.state.ma.us/MHDL/. This list may be updated from time to time.

Drugs Designated for Exclusion from 340B Coverage
Effective for dates of service on or after July 1, 2024, MassHealth has designated certain high-cost drugs as nonpayable when purchased through the 340B drug pricing program and provided to MassHealth ACO members. Each of these drugs is listed on the MassHealth Acute Hospital Carve-Out List discussed in the section above.

Tecartus (brexucabtagene autoleucel) is included in the list of high-cost drugs that are nonpayable when purchased through the 340B drug pricing program and provided to MassHealth ACO members. Accordingly, claims for Tecartus (brexucabtagene autoleucel) must not be submitted with modifier UD.

Note: This policy affects only the method by which specific high-cost drugs may be purchased when provided to MassHealth ACO members and does not impact the use of 340B drugs for other members. The Plan currently pays the actual acquisition cost for such drugs regardless of whether the drug is acquired through the 340B Drug Pricing Program or not. The Plan will continue to pay providers the actual acquisition cost for such drugs after this policy is implemented.

Sources:
- MassHealth All Provider Bulletin 366 (May 2023), as updated by MassHealth All Provider Bulletin 390 (April 2024).
- MassHealth Managed Care Entity Bulletin 114 (April 2024).

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Policy history

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Approval(s):	Technology Assessment Committee: 05/28/2024 (introduced as a new policy).

Not all services mentioned in this policy are covered for all products or employer groups. Coverage is based upon the terms of a member's particular benefit plan which may contain its own specific provisions for coverage and exclusions regardless of medical necessity. Please

consult the product's Evidence of Coverage for exclusions or other benefit limitations applicable to this service or supply. If there is any discrepancy between this policy and a member's benefit plan, the provisions of the benefit plan will govern. However, applicable state mandates take precedence with respect to fully-insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, federal mandates will apply to all plans. For Medicare and Medicaid members, this policy will apply unless Medicare and Medicaid policies extend coverage beyond this policy.