BOSTON MEDICAL CENTER HEALTHNet PLAN

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WELL SENSE HEALTH PLAN

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Medical Policy

CAR T-Cell Therapy to Treat Hematological Malignancies

Policy Number: OCA 3.22
Version Number: 7
Version Effective Date: 05/01/21

Product Applicability	☒ **All Plan+ Products**
Well Sense Health Plan ☒ Well Sense Health Plan	**Boston Medical Center HealthNet Plan** ☒ MassHealth ☒ Qualified Health Plans/ConnectorCare/Employer Choice Direct ☒ Senior Care Options ◊

Notes:
+ Disclaimer and audit information is located at the end of this document.
◊ The guidelines included in this Plan policy are applicable to members enrolled in Senior Care Options only if there are no criteria established for the specified service in a Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) on the date of the prior authorization request. Review the member's product-specific benefit documents at www.SeniorsGetMore.org to determine coverage guidelines for Senior Care Options.

Policy Summary

Autologous immunotherapy with CD19-specific CAR T-cell therapy may be medically necessary to treat B-cell hematological malignancies (leukemia and lymphoma). The clinical regimen must be consistent with National Comprehensive Cancer Network (NCCN) guidance for the treatment of patients with CAR T-cell therapy and applicable guidelines established by the U.S. Food & Drug Administration (FDA) in effect on the date of infusion. When all applicable Plan criteria are met, the Plan considers KYMRIAH® (tisagenlecleucel) to be **medically necessary** to treat members age 25 and younger with refractory or relapse (R/R) B-cell precursor acute lymphoblastic leukemia. KYMRIAH® (tisagenlecleucel) is considered **medically necessary** to treat specific types of large B-cell lymphoma for patients age 18 or

older (as an alternative to YESCARTA®) when all applicable Plan criteria are met and it is a covered treatment for the Plan member. The Plan considers the use of YESCARTA® (axicabtagene ciloleucel) to be **medically necessary** to treat adult members 18 years of age or older with some types of R/R large B-cell lymphoma when all applicable medical necessity criteria are met (as an alternative treatment to KYMRIAH®) and it is a covered treatment for the Plan member. The Plan considers the use of TECARTUS™ (brexucabtagene autoleucel) to be **medically necessary** to treat adult members 18 years of age or older with R/R mantle cell lymphoma when all applicable medical necessity criteria are met and it is a covered treatment for the Plan member.

Prior authorization with Plan Medical Director review and approval is required for every request for CAR T-Cell therapy, including but not limited to the intravenous infusion of KYMRIAH®, YESCARTA®, or TECARTUS™, for any indication (including those indications considered medically necessary in the Medical Policy Statement section of this policy) due to the risk of severe cytokine release syndrome, neurotoxicity, and the potential for other life-threatening complications of CAR T-cell therapy.

Prior authorization requests for types of immunotherapy NOT specified in the Medical Policy Statement section of this policy (including other indications and/or agents for CAR T-cell therapy) will be evaluated for medical necessity using the Plan's *Medically Necessary* medical policy or the *Experimental and Investigational Treatment* medical policy. A Plan Medical Director will evaluate the requested treatment, with individual consideration based on the member's clinical condition and past medical history. Refer to the Plan's *Medically Necessary* medical policy, policy number OCA 3.14, for the product-specific definitions of medically necessary treatment. See the Plan's *Experimental and Investigational Treatment* medical policy, policy number OCA 3.12, for the product-specific definitions of experimental or investigational treatment. Review the Plan's *Genetic/Genomic Testing and Pharmacogenetics* medical policy, policy number OCA 3.727, rather than this policy for genetic testing to identify the member's risk-associated genetic alterations, confirm a diagnosis, estimate treatment response, whole exome sequencing, and/or whole genome sequencing.

Description of Item or Service

Adoptive Immunotherapy (Cellular Adoptive Immunotherapy, Adoptive Cellular Therapy):
Treatment used to activate lymphocytes (specific and/or nonspecific activation) in order to help the patient's immune system fight diseases such as certain cancer and viral infections. Adoptive cancer immunotherapies are developed using different cell types and underlying mechanisms; however, common to all of these products is the goal to induce patient's own immune response against the tumor cells via specific tumor cell recognition and induction of cytotoxicity. Immune cells with antitumor activity are infused into a patient to mediate tumor regression (e.g., CAR T-cell therapy for specific proliferation of lymphocytes). Types of adoptive immunotherapy include the use of adoptive cellular therapy for the administration of cytotoxic T-lymphocytes, cytokine-induced killer cells, tumor-infiltrating lymphocytes, antigen-loaded autologous dendritic cells, or genetically-engineered T-cells.

Chimeric Antigen Receptor T-Cell Therapy (CAR T-Cell Therapy, CAR-T Cell Therapy, CAR-T Therapy, Modified T-Cell Therapy, and Adoptive T-Cell Therapy): A type of customized adoptive immunotherapy in which a patient's own (autologous) T-cells from lymphocytes are harvested from peripheral blood via apheresis and genetically reengineered in the laboratory. The T cells are modified with gene transfer techniques to include a new gene that contains a specific protein (a chimeric antigen receptor or CAR) for the CD19 antigen. CD19 is found in some leukemia and lymphoma cells. Once the cells are modified to become CAR T cells and grown in the laboratory, the genetically modified T cells are infused back into the patient to target cancer cells, selectively targeting and binding to CD19 antigen expressed on the surface of B cells and tumors derived from B cells. Patients receiving CAR T-cell therapy typically have exhausted all other treatment options, including chemotherapy, radiation, or stem cell transplant (as appropriate). CAR T-cell therapy has made remarkable strides in the treatment of patients with B-cell hematological malignancies (leukemia and lymphoma). Success has been limited when used to treat solid tumors due to heterogeneous antigen expression, immunosuppressive networks in the tumor microenvironment limiting CAR T-cell function and persistence, and suboptimal trafficking to solid tumors.

KYMRIAH® (Tisagenlecleucel): KYRMIAH® (drug brand name)/tisagenlecleucel (drug generic name) is a customized treatment for the individual patient that is a cluster of differentiation antigen 19 (CD19)-directed, genetically-modified (adoptive) autologous T-cell immunotherapy. KYMRIAH® is the only CAR T-cell therapy approved by the U.S. Food & Drug Administration (FDA) for two (2) distinct indications - in large B-cell lymphoma and B-cell precursor acute lymphoblastic leukemia (ALL). As of August 2017, KYMRIAH® became the first FDA-approved CAR T-cell therapy for the one-time treatment (in a single administration) for patients 25 years of age and younger with B-cell precursor ALL that is refractory or in second or later relapse, as specified in the Medical Policy Statement section of this policy. KYMRIAH® has also been FDA approved as of May 2018 for the one-time (per patient) use for adults age 18 or older with relapsed or refractory (R/R) large B-cell lymphoma after two (2) or more lines of systemic therapy, as referenced in the Medical Policy Statement section of this policy. KYMRIAH® is NOT indicated for the treatment of patients with primary central nervous system lymphoma and is NOT FDA-approved for R/R primary mediastinal large B-cell lymphoma.

KYMRIAH® is a type of CAR T-cell therapy. Each dose of KYMRIAH® is a customized treatment created from the individual patient's own T cells from lymphocytes. The patient's T-cells are collected from peripheral blood via apheresis and sent to a laboratory where they are modified with gene transfer techniques to include a new gene that contains a specific protein (a chimeric antigen receptor or CAR) for the CD19 antigen. CD19 is found in some leukemia and lymphoma cells. Once the cells are modified to become CAR T cells and grown in the laboratory, the genetically modified T cells are infused back into the patient to target cancer cells, selectively targeting and binding to CD19 antigen expressed on the surface of B cells and tumors derived from B cells.

Treatment with KYMRIAH® has the potential to cause severe side effects, including neurological events and cytokine release syndrome (CRS), a systemic response to the activation and proliferation of CAR T cells causing high fever and flu-like symptoms. Both CRS and neurological events can be life-threatening. Other side effects of KYMRIAH® include but are not limited to serious infections,

hypotension, acute kidney injury, fever, hypoxia, difficulty breathing, confusion, severe muscle or joint pain, dizziness, headache, nausea, vomiting, and diarrhea. Most symptoms appear within 1 to 22 days following infusion of KYMRIAH®. Since the CD19 antigen is also present on normal B-cells, KYMRIAH® will also destroy normal B cells that produce antibodies, and therefore may be an increased risk of infections for a prolonged period of time, including the risk of life-threatening infections that my lead to death. KYMRIAH® in the patient's bloodstream may cause a false-positive HIV test result by some commercial tests.

TECARTUS™ (Brexucabtagene Autoleucel): TECARTUS™ (drug brand name)/brexucabtagene autoleucel (drug generic name) is the first cell-based gene therapy approved by the FDA used for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL). Each dose of TECARTUS™ is a customized treatment using a patient's own immune system. The patient's T cells are collected and genetically modified to include a new gene that facilitates the targeting and killing of the lymphoma cells. These modified T cells are then infused back into the patient. This indication is FDA 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.

YESCARTA®(Axicabtagene Ciloleucel): YESCARTA® (drug brand name)/axicabtagene ciloleucel (drug generic name) is an autologous, CD19-directed genetically modified autologous T-cell immunotherapy indicated for the treatment of adult patients age 18 or older with relapsed or refractory (R/R) large B-cell lymphoma after two (2) or more lines of systemic therapy, 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, as specified in the Medical Policy Statement section of this policy. As of October 2017, FDA has approved the one-time treatment (in a single administration) of YESCARTA® for these indications. YESCARTA® is NOT indicated for the treatment of patients with primary central nervous system lymphoma.

YESCARTA® is a type of CAR T-cell therapy prepared from the patient's peripheral blood mononuclear cells, which are obtained via a standard leukapheresis procedure. A gene for a special receptor called chimeric antigen receptor (CAR) is added to the T cells in the laboratory. These changed T cells called CAR T cells are grown in large numbers in the laboratory and given to the patient by infusion. YESCARTA® binds to a protein called CD19, which is found on most B cell lymphoma cells. The product is thawed prior to infusion and used to help the body's immune system kill cancer cells.

Treatment with YESCARTA® has the potential to cause severe side effects, including neurological events and cytokine release syndrome (CRS), a systemic response to the activation and proliferation of CAR T-cells causing high fever and flu-like symptoms. Both CRS and neurological events can be life-threatening. Other side effects of YESCARTA® include but are not limited to fever, leukopenia, hypoxia, hypotension, tachycardia, cardiac arrhythmias, confusion, difficulty speaking or slurred speech, dizziness, encephalopathy, tremor, fatigue, headache, decreased appetite, chills, nausea, vomiting, diarrhea, constipation, febrile neutropenia, infections-pathogen unspecified, hypoxia, and cough.

Medical Policy Statement

KYMRIAH®/tisagenlecleucel, YESCARTA®/axicabtagene ciloleucel, and TECARTUS™/brexucabtagene autoleucel are listed on the MassHealth Acute Hospital Carve-Out Drugs List and is subject to additional monitoring and billing requirements according to MassHealth guidelines documented at https://masshealthdruglist.ehs.state.ma.us/MHDL/pubtheradetail.do?id=353 for MassHealth Plan members. Utilization Reviewers will be reaching out to providers approximately 30 calendar days after the CAR T-cell infusion date to verify clinical effectiveness and at ongoing intervals for long-term monitoring of sustained response.

The Plan considers the use of ONE (1) of the following U.S. Food & Drug Administration (FDA)-approved CD19-specific CAR T-cell therapies to be medical necessity when infusion occurs in an acute care clinical setting (to closely monitor members for complications and immediately transition to inpatient care when clinically appropriate) and the clinical regimen is consistent with all applicable FDA guidelines (including dosage, administration, indications, and usage) and National Comprehensive Cancer Network (NCCN) guidance for treatment of patients with CAR T-cell therapy for the member's diagnosis in effect on the date of infusion. **When the treatment is covered for the member**, all applicable Plan clinical review criteria must be met and documented in the member's medical record, as specified below in item 1 (for KYMRIAH®/tisagenlecleucel infusion therapy to treat B-cell precursor acute lymphoblastic leukemia), item 2 (for KYMRIAH®/tisagenlecleucel infusion therapy to treat large B-cell lymphoma), item 3 (for YESCARTA®/axicabtagene ciloleucel infusion therapy to treat large B-cell lymphoma), or item 4 (for TECARTUS™/brexucabtagene autoleucel) infusion therapy to treat mantle cell lymphoma):

1. **KYMRIAH® (Tisagenlecleucel) to Treat B-Cell Precursor Acute Lymphoblastic Leukemia**:

   The one-time, single administration of KYMRIAH® (tisagenlecleucel) intravenous infusion is considered medically necessary as second-line therapy for B-cell precursor acute lymphoblastic leukemia when it is a covered/payable treatment for the Plan member and all of the following applicable criteria are met, as specified below in items a through e:

   a. Member is 25 years of age or younger on the date of the infusion (date of service) and KYMRIAH® is prescribed by a hematologist or oncologist; AND

   b. Member has a confirmed CD19-positive B-cell precursor acute lymphoblastic leukemia (by testing or analysis confirming CD19 protein on the surface of the B-cell and documented in the member's medical record) and the member's condition meets ONE (1) of the additional criteria, as specified below in either item (1) or item (2):

      (1) Second or later relapse B-cell precursor acute lymphoblastic leukemia after failing at least two (2) lines of adequate treatment (with relapse defined as the reappearance of leukemia cells in the bone marrow or peripheral blood after complete remission with chemotherapy and/or allogeneic cell transplant); OR

(2) Refractory B-cell precursor acute lymphoblastic leukemia with refractory defined as failure to obtain complete response with induction therapy (with second or later bone marrow relapse, bone marrow relapse after allogeneic stem cell transplant, or primary refractory or chemo-refractory after relapse); AND

c. Member has adequate bone marrow, cardiac, pulmonary, and organ function and deterioration of the member's medical condition is not expected within four (4) weeks after KYMRIAH® intravenous infusion, as determined by the treating oncologist/hematologist and consistent with the clinical guidelines and limitations for treatment specified in the Limitations section of this policy; AND

d. Member has NOT received prior CD19-directed treatment (including but not limited to KYMRIAH®) or any other gene therapy, and the member is NOT being considered for treatment with any other gene therapy; AND

e. The healthcare facility that dispenses and administers KYMRIAH® is enrolled and complies with the KYMRIAH® Risk Evaluation and Mitigation Strategy (REMS) program (described in the Definitions section of this policy and according to all applicable FDA guidelines in effect on the date of service), including but not limited to the administration of adequate prior therapy appropriate for the member's clinical condition with targeted dosage based on the number of CAR-positive viable T cells calculated per kg of body weight and pharmacotherapy for the treatment of cytokine release syndrome if necessary after KYMRIAH® infusion (with immediate access to and the administration of tocilizumab or the appropriate medication according to the dosing and monitoring guidelines specified in the KYMRIAH® REMS program in effect on the date of service); OR

2. **KYMRIAH® (Tisagenlecleucel) to Treat Relapse or Refractory Large B-Cell Lymphoma**: □

The one-time, single administration of KYMRIAH® (tisagenlecleucel) intravenous infusion is considered medically necessary as second-line therapy for large B-cell lymphoma when it is a covered/payable treatment for the Plan member and all of the following applicable criteria are met, as specified below in items a through f:

a. Member is 18 years of age or older on the date of the infusion (date of service) and KYMRIAH® is prescribed by a hematologist or oncologist; AND

b. Member has a confirmed diagnosis of CD19-positive large B-cell lymphoma (by histologically testing or analysis confirming CD19 protein on the surface of the B-cell and documented in the member's medical record), including ANY of the following types, as stated below in items (1) through (3):

(1) Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma; OR

(2) DBCL not otherwise specified; OR

(3) High-grade B-cell lymphoma; AND

c. The member's diagnosis of large B-cell lymphoma meets ONE (1) of the following additional criteria AFTER the member has failed at least two (2) lines of adequate systemic treatment ‡ which **may or may not have included therapy supported by autologous stem cell transplant**, as specified below in either item (1) or item (2):

(1) Second or later relapse B-cell lymphoma; OR

(2) Refractory B-cell lymphoma (with refractory defined as failure to obtain complete response with adequate prior therapy); AND

‡ Note: Adequate therapy includes an anthracycline-containing chemotherapy regimen; for CD20-positive disease, anti-CD20 monoclonal antibody; and for members with transformed follicular lymphoma, prior chemotherapy for follicular lymphoma with chemotherapy refractory disease after transformation to DBCL.

d. Member has adequate bone marrow, cardiac, pulmonary, and organ function with no active autoimmune disease requiring immunosuppression, and deterioration of the member's medical condition is not expected within four (4) weeks after KYMRIAH® intravenous infusion, as determined by the treating oncologist/hematologist and consistent with the clinical guidelines and limitations for treatment specified in the Limitations section of this policy; AND

e. Member has NOT received prior CD19-directed treatment (including but not limited to KYMRIAH® or YESCARTA®) or any other gene therapy, and the member is NOT being considered for treatment with any other gene therapy; AND

f. The healthcare facility that dispenses and administers KYMRIAH® is enrolled and complies with the KYMRIAH® Risk Evaluation and Mitigation Strategy (REMS) program (described in the Definitions section of this policy and according to all applicable FDA guidelines in effect on the date of service), including but not limited to the administration of adequate prior therapy appropriate for the member's clinical condition with targeted dosage based on the number of CAR-positive viable T cells calculated per kg of body weight and pharmacotherapy for the treatment of cytokine release syndrome if necessary after KYMRIAH® infusion (with immediate access to and the administration of tocilizumab or the appropriate medication according to the dosing and monitoring guidelines specified in the KYMRIAH® REMS program in effect on the date of service); OR

3. **YESCARTA® (Axicabtagene Ciloleucel) to Treat Relapse or Refractory B-Cell Lymphoma**:

The one-time, single administration of YESCARTA® (axicabtagene ciloleucel) intravenous infusion is considered medically necessary as second-line therapy for B-cell lymphoma when it is a covered/payable treatment for the Plan member and all of the following applicable criteria are met, as specified below in items a through f:

a. Member is 18 years of age or older on the date of the infusion (date of service) and YESCARTA® is prescribed by a hematologist or oncologist; AND

b. Member has a confirmed diagnosis of CD19-positive large B-cell lymphoma (by histologically testing or analysis confirming CD19 protein on the surface of the B-cell and documented in the member's medical record), including ANY of the following types, as stated below in items (1) through (4):

(1) Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma; OR

(2) DBCL not otherwise specified; OR

(3) High-grade B-cell lymphoma; OR

(4) Primary mediastinal large B-cell lymphoma, AND

c. The member's diagnosis of B-cell lymphoma meets ONE (1) of the following additional criteria AFTER the member has failed at least two (2) lines of adequate systemic treatment‡, as specified below in either item (1) or item (2):

(1) Second or later relapse B-cell lymphoma; OR

(2) Refractory B-cell lymphoma (with refractory defined as failure to obtain complete response with adequate prior therapy); AND

‡ Note: Adequate therapy includes an anthracycline-containing chemotherapy regimen; for CD20-positive disease, anti-CD20 monoclonal antibody; and for members with transformed follicular lymphoma, prior chemotherapy for follicular lymphoma with chemotherapy refractory disease after transformation to DBCL.

d. Member has adequate bone marrow, cardiac, pulmonary, and organ function with no active autoimmune disease requiring immunosuppression, and deterioration of the member's medical condition is not expected within four (4) weeks after YESCARTA® intravenous infusion, as determined by the treating oncologist/hematologist and consistent with the clinical guidelines and limitations for treatment specified in the Limitations section of this policy; AND

e. Member has NOT received prior CD19-directed treatment (including but not limited to YESCARTA® or KYMRIAH®) or any other gene therapy, and the member is NOT being considered for treatment with any other gene therapy; AND

f. The healthcare facility that dispenses and administers YESCARTA® is enrolled and complies with the YESCARTA® Risk Evaluation and Mitigation Strategy (REMS) program (described in the Definitions section of this policy and according to all applicable FDA guidelines in effect on the date of service), including but not limited to the administration of adequate prior therapy appropriate for the member's clinical condition with targeted dosage of the cell suspension for infusion based on the number of CAR-positive viable T cells calculated per kg of body weight and pharmacotherapy for the treatment of cytokine release syndrome if necessary after YESCARTA® infusion (with immediate access to and the administration of tocilizumab or the appropriate medication according to the dosing and monitoring guidelines specified in the YESCARTA® REMS program in effect on the date of service); OR

4. **TECARTUS™ (Brexucabtagene Autoleucel) to Treat Relapsed or Refractory Mantle Cell Lymphoma (MCL)**:

The one-time, single administration of TECARTUS™ (brexucabtagene autoleucel) intravenous infusion is considered medically necessary as second-line therapy for MCL when it is a covered/payable treatment for the Plan member and all of the following applicable criteria are met, as specified below in items a through f:

a. Member is 18 years of age or older on the date of the infusion (date of service) and TECARTUS™ is prescribed by a hematologist or oncologist; AND

b. Member has a confirmed diagnosis of CD19-positive MCL (by histologically testing or analysis confirming CD19 protein on the surface of the B-cell and documented in the member's medical record); AND

c. The member's diagnosis of MCL meets ONE (1) of the following additional criteria AFTER the member has received adequate systemic treatment‡, as specified below in either item (1) or item (2):

(1) Second or later relapse MCL; OR

(2) Refractory MCL (with refractory defined as failure to obtain complete response with adequate prior therapy); AND

‡ Note: Adequate therapy includes all of the following: an anthracycline or bendamustine--containing chemotherapy regimen, anti-CD20 monoclonal antibody (e.g., rituximab),

and a Bruton tyrosine kinase (BTK) inhibitor indicated for mantle cell lymphoma (e.g., acalabrutinib, ibrutinib, zanubrutinib).

d. Member has adequate bone marrow, cardiac, pulmonary, and organ functioning with no active autoimmune disease requiring immunosuppression, and deterioration of the member's medical condition is not expected within four (4) weeks after TECARTUS™ intravenous infusion, as determined by the treating oncologist/hematologist and consistent with the clinical guidelines and limitations for treatment specified in the Limitations section of this policy; AND

e. Member has NOT received prior CD19-directed treatment (including but not limited to TECARTUS™) or any other gene therapy, and the member is NOT being considered for treatment with any other gene therapy; AND

f. The healthcare facility that dispenses and administers TECARTUS™ is enrolled and complies with the TECARTUS™ Risk Evaluation and Mitigation Strategy (REMS) program (described in the Definitions section of this policy and according to all applicable FDA guidelines in effect on the date of service), including but not limited to the administration of adequate prior therapy appropriate for the member's clinical condition with targeted dosage based on the number of CAR-positive viable T cells calculated per kg of body weight and pharmacotherapy for the treatment of cytokine release syndrome if necessary after TECARTUS™ infusion (with immediate access to and the administration of tocilizumab or the appropriate medication according to the dosing and monitoring guidelines specified in the TECARTUS™ REMS program in effect on the date of service).

Limitations

ANY of the following are limitations related to chimeric antigen receptor (CAR) T-cell therapy, as specified below in items 1 through 3:

1. **Plan Medical Director Review**:

   a. Prior authorization with Plan Medical Director review and approval with individual consideration is required for the use of KYMRIAH® (tisagenlecleucel), YESCARTA® (axicabtagene ciloleucel), or TECARTUS™ (brexucabtagene autoleucel)for **any indication** (including those considered medically necessary in the Medical Policy Statement section of this policy) due to the risk of severe cytokine release syndrome, neurotoxicity, and the potential for other life-threatening complications of CAR T-cell therapy.

   b. Plan Medical Director review with individual consideration is required for the use of modified T-cell immunotherapies and adoptive immunotherapy NOT specified in the Medical Policy Statement, treatment that is NOT for an FDA label indication for the administration of KYMRIAH® (tisagenlecleucel), YESCARTA® (axicabtagene ciloleucel), or

TECARTUS™ (brexucabtagene autoleucel) and/or for an indication NOT stated in the Medical Policy Statement section of this policy. Examples of indications not FDA approved for this treatment include but are not limited to any of the following conditions: AIDS-related B-cell lymphoma, human herpes virus 8-positive diffuse large B-cell lymphoma, post-transplant lymphoproliferative disorders (B-cell type), and/or the use of CAR T-cell therapy with solid tumors.

c. Plan Medical Director review with individual consideration is required for the use of KYMRIAH® (tisagenlecleucel) to treat primary mediastinal B-cell lymphoma when all other applicable medical necessity criteria included in the Medical Policy Statement section are met (excluding refractory or relapsed primary mediastinal large B-cell lymphoma). KYMRIAH® is not FDA approved for the treatment of primary mediastinal B-cell lymphoma. A contraindication for the use of KYMRIAH® intravenous infusion includes refractory or relapsed primary mediastinal large B-cell lymphoma, as specified below.

2. **Contraindications**:

a. Contraindications for KYMRIAH® (Tisagenlecleucel):

Contraindications to treatment a member with KYMRIAH® (tisagenlecleucel) intravenous infusion include ANY of the following conditions, as specified below in items (1) through (12):

(1) Active central nervous system (CNS) group 3 acute lymphoblastic leukemia (see the Definitions section of this policy for a definition of Central Nervous System (CNS) Involvement in Acute Lymphoblastic Leukemia (ALL); OR

(2) Active and/or metastatic malignancy (other than the condition specified as medically necessary in the Medical Policy Statement section of this policy); OR

(3) Allogeneic cellular therapy (e.g., donor lymphocyte infusion) received within six (6) weeks prior to the requested KYMRIAH® (tisagenlecleucel) infusion; OR

(4) Autoimmune disorder requiring immunosuppression, immunodeficiency syndrome, or active and uncontrolled infection (including but not limited to active hepatitis B, active hepatitis C); OR

(5) Burkitt lymphoma; OR

(6) Central nervous system disease (CNS), including but not limited to brain metastases, CNS lymphoma, and/or a history or presence of CNS disorders such as cerebrovascular ischemia/hemorrhage, cerebellar disease, dementia, seizure disorder; OR

(7) Graft-versus-host disease grade 2 to 4; OR

(8) Human immunodeficiency virus (HIV); OR

(9) Pregnancy or breastfeeding; OR

(10) Prior treatment with CAR T-cell therapy or other type of modified T-cell therapy; OR

(11) Refractory or relapsed primary mediastinal large B-cell lymphoma (with refractory or relapsed primary mediastinal large B-cell lymphoma defined as progression after two [2] or more lines of systemic therapy which may or may not include therapy supported by autologous cell transplant); OR

(12) Use in combination with other chemotherapy agents (NOT specified in the Medical Policy Statement section).

b. Contraindications for YESCARTA® (Axicabtagene Ciloleucel):

Contraindications to treating a member with YESCARTA® (axicabtagene ciloleucel) intravenous infusion include ANY of the following conditions, as specified below in items (1) through (8):

(1) Active and/or metastatic malignancy (other than the condition specified as medically necessary in the Medical Policy Statement section of this policy); OR

(2) Autoimmune disorder, immunodeficiency syndrome, or active and uncontrolled infection (including but not limited to active hepatitis B, active hepatitis C); OR

(3) Central nervous system disease (CNS), including but not limited to brain metastases, CNS lymphoma, and/or a history or presence of CNS disorders such as cerebrovascular ischemia/hemorrhage, cerebellar disease, dementia, seizure disorder; OR

(4) Graft-versus-host disease; OR

(5) Human immunodeficiency virus (HIV); OR

(6) Pregnancy or breastfeeding; OR

(7) Primary central nervous system (CNS) lymphoma; OR

(8) Prior treatment with CAR T-cell therapy, other type of modified T-cell therapy, and/or allogeneic stem cell transplant.

c. Contraindications for TECARTUS™ (Brexucabtagene Autoleucel):

Contraindications to treating a member with TECARTUS™ (brexucabtagene autoleucel) intravenous infusion include ANY of the following conditions, as specified below in items (1) through (7):

(1) Active and/or metastatic malignancy (other than the condition specified as medically necessary in the Medical Policy Statement section of this policy); OR

(2) Autoimmune disorder, immunodeficiency syndrome, or active and uncontrolled infection (including but not limited to active hepatitis B, active hepatitis C); OR

(3) Central nervous system disease (CNS), including but not limited to brain metastases, CNS lymphoma, and/or a history or presence of CNS disorders such as cerebrovascular ischemia/hemorrhage, cerebellar disease, dementia, seizure disorder; OR

(4) Graft-versus-host disease; OR

(5) Human immunodeficiency virus (HIV); OR

(6) Pregnancy or breastfeeding; OR

(7) Prior treatment with CAR T-cell therapy, other type of modified T-cell therapy, and/or allogeneic stem cell transplant.

3. **Experimental and Investigational**:

a. KYMRIAH® (Tisagenlecleucel):

ANY of the following indications for treatment with KYMRIAH® (tisagenlecleucel) is considered experimental and investigational, as specified below in item (1) or item (2):

(1) The Plan considers repeat administration of KYMRIAH® (tisagenlecleucel) to be experimental and investigational because the effectiveness of a repeated administration for this treatment has NOT been established; OR

(2) The Plan considers KYMRIAH® (tisagenlecleucel) experimental and investigational for ANY of the following indications (not an all-inclusive list) because its effectiveness for these indications has not been established, as specified below in items (a) through (k):

(a) Acute myeloid leukemia; OR

(b) Adult members age 26 or older on the date of infusion (date of service) with refractory or second relapse B-cell precursor acute lymphoblastic leukemia; OR

(c) Chronic lymphocytic leukemia; OR

(d) Hodgkin lymphoma; OR

(e) Pediatric members age 17 or younger on the date of infusion (date of service) with large B-cell lymphoma; OR

(f) Plasma cell disorders (e.g., multiple myeloma); OR

(g) Primary central nervous system lymphoma; OR

(h) Relapsed or refractory primary mediastinal large B-cell lymphoma; OR

(i) Solid tumors (e.g., glioma, glioblastoma and neuroblastoma); OR

(j) T-cell leukemia/lymphoma (e.g., acute T-cell leukemia, adult T-cell leukemia/lymphoma, anaplastic large-cell lymphoma, and cutaneous T cell lymphoma); OR

(k) Any indication NOT specified as medically necessary in the Medical Policy Statement section of this policy.

b. YESCARTA® (Axicabtagene Ciloleucel):

ANY of the following indications for treatment with YESCARTA® (axicabtagene ciloleucel) is considered experimental and investigational, as specified below in item (1) or item (2):

(1) The Plan considers repeat administration of YESCARTA® (axicabtagene ciloleucel) to be experimental and investigational because the effectiveness of a repeated administration for this treatment has NOT been established; OR

(2) The Plan considers YESCARTA® (axicabtagene ciloleucel) experimental and investigational for ANY of the following indications (not an all-inclusive list) because its effectiveness for these indications has not been established, as specified below in items (a) and (b):

(a) Pediatric members age 17 and younger on the date of infusion (date of service) with relapsed or refractory B-cell lymphoma; OR

(b) Any indication NOT specified as medically necessary in the Medical Policy Statement section of this policy.

c. TECARTUS™ (Brexucabtagene Autoleucel)

ANY of the following indications for treatment with TECARTUS™ (brexucabtagene autoleucel) is considered experimental and investigational, as specified below in item (1) or item (2):

(1) The Plan considers repeat administration of TECARTUS™ (brexucabtagene autoleucel) to be experimental and investigational because the effectiveness of a repeated administration for this treatment has NOT been established; OR

(2) The Plan considers TECARTUS™ (brexucabtagene autoleucel) experimental and investigational for ANY of the following indications (not an all-inclusive list) because its effectiveness for these indications has not been established, as specified below in items (a) and (b):

(a) Pediatric members age 17 and younger on the date of infusion (date of service) with relapsed or refractory mantle cell lymphoma; OR

(b) Any indication NOT specified as medically necessary in the Medical Policy Statement section of this policy.

d. Other Types of CAR T-Cell Therapy:

All other types of CAR T-Cell therapy NOT specified in the Medical Policy Statement section of this policy are considered experimental and investigational, including but NOT limited to the use of idecabtagene vicleucel as a proposed treatment of adults with relapsed/refractory multiple myeloma.

Prior authorization requests for types of immunotherapy (or other indications for CAR T-cell therapy) NOT specified in the Medical Policy Statement section of this policy will be evaluated for medical necessity using the Plan's *Medically Necessary* medical policy or the *Experimental and Investigational Treatment* medical policy. A Plan Medical Director will evaluate the requested treatment, with individual consideration based on the member's clinical condition and past medical history. Refer to the Plan's *Medically Necessary* medical policy, policy number OCA 3.14, for the product-specific definitions of medically necessary treatment. See the Plan's *Experimental and Investigational Treatment* medical policy, policy number OCA 3.12, for the product-specific definitions of experimental or investigational treatment. Review the Plan's *Genetic/Genomic Testing and Pharmacogenetics* medical policy, policy number OCA 3.727, rather than this policy for genetic testing to identify the member's risk-associated genetic alterations, confirm a diagnosis, estimate treatment response, whole exome sequencing, and/or whole genome sequencing.

Definitions

Acute Lymphoblastic Leukemia (ALL, Acute Lymphocytic Leukemia): Aggressive type of leukemia characterized by the presence of too many T and B lymphoblasts or lymphocytes in the bone marrow and peripheral blood, replacing and overcrowding the normal hematopoietic cells. It can spread to the lymph nodes, spleen, liver, central nervous system, and other organs. Leukostasis (white cell plugs in microvasculature) affecting brain and lung may also occur. Without treatment, ALL usually progresses quickly. The National Cancer Institute estimates that approximately 3,100 patients aged 20 and younger are diagnosed with ALL each year. ALL can be of either T- or B-cell origin, with B-cell the most common. ALL is the most common type of cancer in children, representing more than a quarter of all pediatric cancers. Approximately 98% of children treated promptly with current regimens attain remission, with long-term and event-free survival rates 90% at 5 years. For adults, the prognosis is less favorable. Signs and symptoms of ALL include but are not limited to fever, weakness or feeling tired, fever or night sweats, easy bruising or bleeding, petechiae, bone or joint pain, loss of appetite, and/or swollen lymph nodes. Tests used to diagnosis ALL include physical exam and history; complete blood count with differential; blood chemistry studies; peripheral blood smears to evaluate characteristics (i.e., type, shape, and amount) of blast cells, white blood cells, platelets, red blood cells, and hemoglobin; and bone marrow aspiration and biopsy. Additional testing may include cytogenetic analysis, immunophenotyping, lumbar puncture, and/or chest x-ray. Treatment options are determined after evaluating patient-specific factors such as age at diagnosis, clinical presentation and risk stratification related to ALL, past medical and treatment history, and whether the leukemia cells originated from B lymphocytes or T lymphocytes. Patients with refractory or relapsed (R/R) ALL have a high risk of relapse. Currently, bone marrow transplant is the only cure for R/R ALL, but many patients are not eligible for transplant based on the patient's age or progression of the disease. The generation of CAR T-cells to treat ALL represents a significant advance in the treatment of ALL. KYMRIAH® (tisagenlecleucel) is approved for use in patients age 25 and younger with B-cell ALL and is intended for patients whose cancer has not responded to or has returned after initial treatment, which occurs in an estimated 15-20% of patients.

B-Cell Lymphomas: Lymphomas that originate from B lymphocytes (rather than T lymphocytes). B-cell lymphomas account for 85% of the cases of non-Hodgkin lymphoma in the United States and are categorized by characteristics such as B-cell microscopic appearance, proteins generated and genetic composition. Types of B-cell lymphomas include but are not limited to diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma, mantle cell lymphoma (MCL), marginal zone B-cell lymphoma, Burkitt lymphoma, and lymphoplasmacytic lymphoma.

B-Cell Precursor Acute Lymphoblastic Leukemia (Precursor B-Lymphoblastic Leukemia, B-Cell Acute Lymphocytic Leukemia): Aggressive, fast-growing type of acute lymphoblastic leukemia (ALL) in which too many B-cell lymphoblasts are present in the bone marrow and blood. Precursor B-cell lymphoblastic leukemia is the most common type of ALL. Signs and symptoms of B-cell precursor ALL include bone pain, arthritis, limping, fevers (low or high), neutropenia, fatigue, pallor, petechiae, bleeding, lymphadenopathy, and/or hepatosplenomegaly.

Burkitt Lymphoma (BL): Highly aggressive type of B-cell non-Hodgkin lymphoma characterized by the translocation and deregulation of the c-MYC gene on chromosome 8.

Central Nervous System (CNS) Involvement in Acute Lymphoblastic Leukemia (ALL): Symptoms of CNS involvement are rarely noted at initial diagnosis for ALL but are more common in T-lineage ALL and mature B cell ALL, and less common with B-cell precursor ALL. CNS disease is divided into the following groups:

1. CNS 1: Absence of blasts on CSF cytospin preparation, regardless of the white blood cell (WBC) count.

2. CNS 2: WBC count of less than 5/mL and blasts on cytospin findings, or WBC count of more than 5/mL but negative by Steinherz-Bleyer algorithm findings (if traumatic tap).

3. CNS 3: WBC count of 5/mL or more and blasts on cytospin findings and/or clinical signs of CNS leukemia (e.g., facial nerve palsy, brain/eye involvement, hypothalamic syndrome).

Cytokine Release Syndrome (CRS): Clinical condition characterized by symptoms that include fever, nausea, fatigue, myalgia, malaise, hypotension, hypoxia, coagulopathy and capillary leak, and/or multi-organ toxicity. CRS is not restricted to CAR T-cell therapy, but CRS has been reported to occur in 30–94% of patients receiving CAR T-cell therapy. CRS typically occurs 1 to 22 days after CAR T-cell infusion, with severe CRS usually occurring earlier in the treatment regimen than less severe CRS. Patients with severe CRS can experience significant hemodynamic instability and capillary leak with hypotension, tachycardia, hypoxia, tachypnea, hemophagocytic lymphohistiocytosis/macrophage activation syndrome, and/or other organ toxicity. Mild-to moderate CRS usually can be managed with close observation and supportive care. Severe CRS, including fatal or life-threatening reactions, may occur in patients receiving CAR T-Cell therapy that includes intravenous infusion of KYMRIAH®, YESCARTA®, or TECARTUS™.

Diffuse Large B-Cell Lymphoma (DLBCL): The most prevalent and fast-growing, aggressive form of non-Hodgkin lymphoma (NHL). This lymphoma affects patients of all age groups; with the median age at presentation is about 60 years with a slight preponderance for individuals with male reproductive organs. Up to 50% of patients present with advanced disease. Approximately 70% of these lymphomas occur nodal, and the remaining 30% are extranodal. DLBCL can involve any organ, with the most common sites being the gastrointestinal tract, Waldeyer's ring, skin, cerebrum, mediastinum, testis, salivary gland, thyroid and bone. DLBCL is the most common type of high grade NHL and is fatal if left

untreated; when treated promptly with current clinical regimens, approximately two-thirds of all patients can be cured. For patients who relapse or don't respond to initial therapy, there are limited treatment options that provide durable responses, and median life expectancy is approximately six (6) months. Treatment is based on the DLBCL subtype based on molecular classification.

Follicular Lymphoma (FL): Previously called follicle center lymphoma and nodular lymphoma, FL is the second most common subtype of non-Hodgkin lymphoma that includes tumors derived from germinal center B cells with a growth pattern that is partially follicular (i.e., nodular in appearance).

Graft-Versus-Host Disease: Multisystem disorders that are common complications when immune cells transplanted from a non-identical donor (the graft) recognize the transplant recipient (the host) as foreign, resulting in an immune reaction that causes disease in the transplant recipient. Several systems for grading acute graft-versus-host disease (GVHD) have been developed. The two most popular are the Glucksberg grade (I-IV) and the International Bone Marrow Transplant Registry (IBMTR) grading system (A-D). The severity of acute GVHD is determined by an assessment of the degree of involvement of the skin, liver, and gastrointestinal tract. Grade I(A) GVHD is characterized as mild disease, grade II(B) GVHD as moderate, grade III(C) as severe, and grade IV(D) life-threatening.

High-Grade B-Cell Lymphoma (HGBL): Previously called double-hit or triple-hit diffuse large B-cell lymphoma (DLBCL), the disease presents with features intermediate between DLBCL and Burkitt lymphoma and therefore is difficult to categorize. Condition presents with specific high-grade morphology (gene rearrangements) and an aggressive clinical presentation.

Immunotherapy for Cancer Treatment: A type of treatment that utilizes the body's own immune system to fight cancer, using immune cells or antibodies to detect and kill cancer cells. Immune cells or antibodies can be produced in the laboratory under tightly controlled conditions and then given to patients to treat cancer. Several types of immunotherapy are either approved by the U.S. Food & Drug Administration (FDA) or are under study in clinical trials to determine their effectiveness in treating various types of cancer, including CAR T-cell therapy.

KYMRIAH® Risk Evaluation and Mitigation Strategy (KYMRIAH® REMS): Mandatory program required by the U.S. Food & Drug Administration (FDA) to administer KYMRIAH® (tisagenlecleucel) in order to manage the known and potential serious risks associated with the therapy and to ensure that the benefits of treatment outweigh its risks. The goals of the KYMRIAH® REMS program are to mitigate the risks of cytokine release syndrome (CRS) and neurological toxicities by: (1) ensuring that hospitals and facilities that dispense KYMRIAH® are specially certified and have on-site, immediate access to tocilizumab with a minimum of two (2) doses of tocilizumab available for each patient for administration within two (2) hours after KYMRIAH® infusion; and (2) requiring that providers who prescribe, dispense, and/or administer KYMRIAH® are trained to both identify the risks associated with CRS and neurological toxicities and to effectively treat these potentially life-threatening conditions when they occur, including the administration of tocilizumab or tocilizumab and corticosteroids for CRS and support care for neurological events. KYMRIAH® should NOT be administered to patients with

active infection or inflammatory disorders. KYMRIAH® is available only through a restricted KYMRIAH® REMS program.

Lymphocytes: A subtype of white blood cells that plays a larger role in the body's immune system. There are two (2) main types of lymphocytes: B cells and T cells. The B cells make antibodies that attack bacteria and toxins; T cells attack body cells themselves when they have been taken over by viruses or have become cancerous.

Lymphoma: Cancer of lymphocytes. Lymphocytes circulate throughout the body via the lymphatic system, which includes the bone marrow, spleen, thymus, and lymph nodes connected by a network of lymphatic and blood vessels. There are two (2) main types of lymphoma, Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). NHL is the most common type of lymphoma, and diffuse large B cell lymphoma (DLBCL) is the most prevalent form of NHL.

Mantle Cell Lymphoma (MCL): MCL is a type of B cell non-Hodgkin lymphoma. The cancerous B cells are within a region of the lymph node known as the mantle zone. Although MCLs are slow-growing cancers, the cancer is usually widespread when diagnosed and can become life-threatening shortly after diagnosis. Treatment of MCL is not curative and nearly all patients will have refractory or recurrent MCL.

Non-Hodgkin Lymphoma (Non-Hodgkin's Lymphoma, NHL, Lymphoma): Cancer that starts in the lymphocytes, originating in either B cell lymphocytes or T-cell lymphocytes. There are more than 60 types of NHL with various methods of classifying NHL, including the origin of the condition in B lymphocytes (B cells) or T lymphocytes (T cells).

Primary Mediastinal Large B-Cell Lymphoma (PMBL): An aggressive type of B-cell lymphoma that is thought to arise from thymic (medullary) B cells. This lymphoma, which starts in the space between the lungs (the mediastinum), is treated like early stage diffuse large B-cell lymphoma. It has clinicopathologic features that are distinct from systemic diffuse large B-cell lymphoma (DLBCL) and shares some features found with classical nodular sclerosing Hodgkin lymphoma (HL). PMBL accounts for 7% of DLBCL and is more prominent with patients with female reproductive organs with a median age of 30's to 40's at the time of diagnosis. If there is a recurrence of primary mediastinal B cell lymphoma or the member does not respond to chemotherapy, immunotherapy may be a medically necessary treatment option.

TECARTUS™ Risk Evaluation and Mitigation Strategy (REMS): Mandatory program required by the U.S. Food & Drug Administration (FDA) to administer TECARTUS™ (brexucabtagene autoleucel) in order to manage the known and potential serious risks associated with the therapy and to ensure that the benefits of treatment outweigh its risks. The goals of the TECARTUS™ REMS program are to mitigate the risks of cytokine release syndrome (CRS) and neurological toxicities. Providers who prescribe, dispense, and/or administer TECARTUS™ must be are trained to both identify the risks associated with CRS and neurological toxicities and to effectively treat these potentially life-threatening conditions when they occur. TECARTUS™ is available only through a restricted TECARTUS™ REMS program.

YESCARTA® Risk Evaluation and Mitigation Strategy (REMS): Mandatory program required by the U.S. Food & Drug Administration (FDA) to administer YESCARTA® (axicabtagene ciloleucel) in order to manage the known and potential serious risks associated with the therapy and to ensure that the benefits of treatment outweigh its risks. The goals of the YESCARTA® REMS program are to mitigate the risks of cytokine release syndrome (CRS) and neurological toxicities by: (1) ensuring that hospitals and facilities that dispense YESCARTA® are specially certified and have on-site, immediate access to tocilizumab with a minimum of two (2) doses of tocilizumab available for each patient for administration within two (2) hours after YESCARTA® infusion; and (2) requiring that providers who prescribe, dispense, and/or administer YESCARTA® are trained to both identify the risks associated with CRS and neurological toxicities and to effectively treat these potentially life-threatening conditions when they occur, including the administration of tocilizumab or tocilizumab and corticosteroids for CRS and support care for neurological events. YESCARTA® should NOT be administered to patients with active infection or inflammatory disorders. YESCARTA® is available only through a restricted YESCARTA® REMS program.

Applicable Coding

The Plan uses and adopts up-to-date Current Procedural Terminology (CPT) codes from the American Medical Association (AMA), International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10) diagnosis codes developed by the World Health Organization and adapted in the United Stated by the National Center for Health Statistics (NCHS) of the Centers for Disease Control under the U.S. Department of Health and Human Services, and the Health Care Common Procedure Coding System (HCPCS) established and maintained by the Centers for Medicare & Medicaid Services (CMS). Since the AMA, NCHS, and CMS may update codes more frequently or at different intervals than Plan policy updates, the list of applicable codes included in this Plan policy is for informational purposes only, may not be all inclusive, and is subject to change without prior notification. Whether a code is listed in the Applicable Coding section of this Plan policy does not constitute or imply member coverage or provider reimbursement. Providers are responsible for reporting all services using the most up-to-date industry-standard procedure and diagnosis codes as published by the AMA, NCHS, and CMS at the time of the service.

Providers are responsible for obtaining prior authorization for the services specified in the Medical Policy Statement section and Limitation section of this Plan policy, even if an applicable code appropriately describing the service that is the subject of this Plan policy is not included in the Applicable Coding section of this Plan policy. Coverage for services is subject to benefit eligibility under the member's benefit plan. Refer to the member's benefits document in effect at the time of the service to determine coverage or non-coverage as it applies to an individual member. Review the Plan's reimbursement policies for Plan billing guidelines. The member's benefit documents and the Plan's policies are available at www.bmchp.org for a BMC HealthNet Plan member, at www.SeniorsGetMore.org for a Senior Care Options member, and at www.wellsense.org for a Well Sense Health Plan member.

HCPCS Codes	Description: Codes Considered Medical Necessary for All Plan Products for CAR T-Cell Therapy Harvesting and Administration
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

HCPCS Code	Description: Codes Considered Medical Necessary for All Plan Products for YESCARTA® (CAR T-Cell Agent)
Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-cd19 car positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose Plan note: This agent is listed on the MassHealth Acute Hospital Carve-Out Drugs List and is subject to additional monitoring and billing requirements according to MassHealth guidelines for MassHealth Plan members, as stated at https://masshealthdruglist.ehs.state.ma.us/MHDL/pubtheradetail.do?id=353. Utilization Reviewers will be reaching out to providers approximately 30 calendar days after the CAR T-cell infusion date to verify clinical effectiveness and at ongoing intervals for long-term monitoring of sustained response.

HCPCS Code	Description: Code Considered Medical Necessary for All Plan Products for KYMRIAH® (CAR T-Cell Agent)
Q2042	Tisagenlecleucel, up to 600 million car-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose Plan note: This agent is listed on the MassHealth Acute Hospital Carve-Out Drugs List and is subject to additional monitoring and billing requirements according to MassHealth guidelines for Plan MassHealth members, as stated at https://masshealthdruglist.ehs.state.ma.us/MHDL/pubtheradetail.do?id=353. Utilization Reviewers will be reaching out to providers approximately 30 calendar days after the CAR-T infusion date to verify clinical effectiveness and at ongoing intervals for long-term monitoring of sustained response.

HCPCS Code	Description: Codes Considered Medical Necessary for All Plan Products for TECARTUS™ (CAR T-Cell Agent)
Q2053	Brexucabtagene autoleucel, up to 200 million autologous anti-cd19 car positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose Plan note: This agent is listed on the MassHealth Acute Hospital Carve-Out Drugs List and is subject to additional monitoring and billing requirements according to MassHealth guidelines for Plan MassHealth members, as stated at https://masshealthdruglist.ehs.state.ma.us/MHDL/pubtheradetail.do?id=353. Utilization Reviewers will be reaching out to providers approximately 30 calendar days after the CAR-T infusion date to verify clinical effectiveness and at ongoing intervals for long-term monitoring of sustained response.

Clinical Background Information

Lymphoma and leukemia share a common origin—lymphocytes, the white blood cells that originate in the bone marrow. B-cells mature in the bone marrow, while T-cells mature in the thymus. These cells, which play critical roles in the immune system, travel through the lymphatic system and bloodstream to protect the body from disease-causing organisms and substances. Chimeric antigen receptor T-cell therapy (CAR T-cell therapy) is a type of customized treatment in which a patient's autologous T-cells are harvested from peripheral blood via apheresis and genetically reengineered in the laboratory to contain a specific protein (a chimeric antigen receptor or CAR) that will bind with a protein on the patient's cancer cells. Autologous immunotherapy with CD19-specific CAR T-cell therapy is used to treat B-cell hematological malignancies (leukemia and lymphoma) when the clinical regimen is consistent with guidelines established by the U.S. Food & Drug Administration (FDA) and National Comprehensive Cancer Network (NCCN) guidance for treatment of patients with CAR T-cell therapy for the member's diagnosis in effect on the date of infusion.

As of August 2017, KYMRIAH® (tisagenlecleucel) became the first CD19-specific CAR T-therapy approved by the FDA for the one-time (per patient) treatment of patients 25 years of age and younger with B-cell precursor acute lymphoblastic leukemia that is refractory or in second or later relapse. Beginning in May 2018, KYMRIAH® has also been FDA approved for the one-time (per patient) use with adults age 18 or older with relapsed or refractory (R/R) large B-cell lymphoma after two (2) 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). In October 2017, YESCARTA® (axicabtagene ciloleucel) became the second CAR T-cell therapy approved by the FDA. YESCARTA® is indicated for patients with large B-cell lymphoma whose cancer has progressed after receiving at least two prior treatment regimens; large B-cell lymphomas include diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, and transformed follicular lymphoma. On July 24, 2020, the FDA approved TECARTUS™ (brexucabtagene autoleucel) as a genetically modified autologous T cell immunotherapy used for the treatment of adult patients with relapse or refractory mantle cell lymphoma.

At the time of the Plan's most recent policy review, no Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) was found for autologous immunotherapy with CD19-specific chimeric antigen receptor T-cell therapy (CAR-T cell therapy, CAR-T therapy, modified T-cell therapy) to treat hematological malignancies. On February 15, 2019 CMS developed a proposed NCD for Chimeric Antigen Receptor (CAR) T-cell Therapy for Cancers to cover autologous treatment with T-cells expressing at least one chimeric antigen receptor (CAR) through coverage with evidence development (CED) when prescribed by the treating oncologist, performed in a hospital, and applicable medical necessity criteria are met. Verify CMS criteria in the applicable NCD or local coverage determination (LCD) in effect for this service on the date of the prior authorization request for a Senior Care Options member.

The CMS NCD for Autologous Cellular Immunotherapy Treatment, NCD # 110.22, covers another type and indication for immunotherapy NOT applicable to this Plan medical policy. NCD # 110.22 states "that the evidence is adequate to conclude that the use of autologous cellular immunotherapy treatment - sipuleucel-T; PROVENGE® improves health outcomes for Medicare beneficiaries with asymptomatic or minimally symptomatic metastatic castrate-resistant (hormone refractory) prostate cancer, and thus is reasonable and necessary for this on-label indication under 1862(a) (1) (A) of the Social Security Act." The medical necessity of this treatment will be determined based on the Plan's *Medically Necessary* medical policy, policy number OCA 3.14, rather than this policy.

Prior authorization requests for types of immunotherapy (or other indications for CAR T-cell therapy) NOT specified in the Medical Policy Statement section of this policy will be evaluated for medical necessity based on the requested treatment and the member's clinical condition using the Plan's *Medically Necessary* medical policy or the *Experimental and Investigational Treatment* medical policy. A Plan Medical Director will evaluate the requested treatment, with individual consideration based on the member's clinical condition and past medical history. Refer to the Plan's *Medically Necessary* medical policy, policy number OCA 3.14, for the product-specific definitions of medically necessary treatment. See the Plan's *Experimental and Investigational Treatment* medical policy, policy number OCA 3.12, for the product-specific definitions of experimental or investigational treatment. Review the Plan's *Genetic/Genomic Testing and Pharmacogenetics* medical policy, policy number OCA 3.727, rather than this policy for genetic testing to identify the member's risk-associated genetic alterations, confirm a diagnosis, estimate treatment response, whole exome sequencing, and/or whole genome sequencing.

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Policy History

Original Approval Date	Original Effective Date* and Version Number	Policy Owner	Original Policy Approved by
Regulatory Approval: N/A Internal Approval: 10/17/18: Medical Policy, Criteria, and Technology Assessment Committee (MPCTAC)	01/01/19 Version 1	Medical Policy Manager as Chair of MPCTAC	MPCTAC

Policy title from 01/01/19 to 04/20/21 was *CAR T-Cell Therapy with KYMRIAH® or YESCARTA® to Treat Hematological Malignancies*. As of 05/01/21, policy title changed to *CAR T-Cell Therapy to Treat Hematological Malignancies*.

Policy Revisions History			
Review Date	**Summary of Revisions**	**Revision Effective Date and Version Number**	**Approved by**
12/01/18	Review for effective date 01/01/19. Industry-wide updates made to the code list in the Applicable Coding section.	01/01/19 Version 2	12/19/18: MPCTAC
09/01/19	Review for effective date 12/01/19. Revised criteria in the Medical Policy Statement and Limitations sections. Administrative changes made to the Definitions, Clinical Background Information, References, and Reference to Applicable Laws and Regulations sections.	12/01/19 Version 3	09/18/19: MPCTAC
07/01/20	Review for effective date 08/01/20. Administrative changes made to the Limitations and References sections.	08/01/20 Version 4	07/15/20: MPCTAC
11/01/20	Review for effective date 12/01/20. Administrative changes made to the Medical Policy Statement and References sections. Plan notes added to the Applicable Coding section.	12/01/20 Version 5	11/18/20: MPCTAC
02/01/21	Review for effective date 05/01/21. Administrative changes made to the Policy Summary, Description of Item or Service, Definitions, Clinical Background Information, and References sections. Criteria revised in the Medical Policy Statement and Limitations sections. Coding and Plan notes updated in the Applicable Coding section. Revised policy title.	05/01/21 Version 6	02/17/21: MPCTAC
03/01/21	Review for effective date 05/01/21. Industry-wide code revisions made for TECARTUS for all Plan products and Plan notes revised in the Applicable Coding section.	05/01/21 Version 7	03/17/21: MPCTAC

Last Review Date

03/01/21

Next Review Date

07/01/21

Authorizing Entity

MPCTAC

Other Applicable Policies

Medical Policy - *Experimental and Investigational Treatment,* policy number OCA 3.12
Medical Policy - *Genetic/Genomic Testing and Pharmacogenetics,* policy number OCA 3.727
Medical Policy - *Medically Necessary*, policy number OCA 3.14
Reimbursement Policy - *General Billing and Coding Guidelines*, policy number 4.31
Reimbursement Policy - *General Billing and Coding Guidelines*, policy number SCO 4.31
Reimbursement Policy - *General Billing and Coding Guidelines*, policy number WS 4.17
Reimbursement Policy - *General Clinical Editing and Payment Accuracy Review Guidelines*, policy number 4.108
Reimbursement Policy - *General Clinical Editing and Payment Accuracy Review Guidelines*, policy SCO 4.108
Reimbursement Policy - *General Clinical Editing and Payment Accuracy Review Guidelines*, policy number WS 4.18
Reimbursement Policy - *Hospital*, policy number WS 4.21
Reimbursement Policy - *Inpatient Hospital*, policy number 4.110
Reimbursement Policy - *Inpatient Hospital*, policy number SCO 4.110
Reimbursement Policy - *Non-Participating Provider,* policy number WS 4.5
Reimbursement Policy - *Non-Reimbursed Codes*, policy number 4.38
Reimbursement Policy - *Non-Reimbursed Codes*, policy number WS 4.38
Reimbursement Policy - *Outpatient Hospital*, policy number 4.17
Reimbursement Policy - *Outpatient Hospital*, policy number SCO 4.17
Reimbursement Policy - *Physician and Non Physician Practitioner Services*, policy number 4.608
Reimbursement Policy - *Physician and Non Physician Practitioner Services*, policy number SCO 4.608
Reimbursement Policy - *Physician and Non Physician Practitioner Services*, policy number WS 4.28
Reimbursement Policy - *Provider Preventable Conditions and Serious Reportable Events*, policy number 4.610
Reimbursement Policy - *Provider Preventable Conditions and Serious Reportable Events*, policy number SCO 4.610
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Reference to Applicable Laws and Regulations

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21 CFR 600.14. Code of Federal Regulations. Food and Drugs. Food and Drug Administration. Department of Health and Human Services. Biologics. Biological Products: General. Established Standards.

21 CFR 601.14. Code of Federal Regulations. Food and Drugs. Food and Drug Administration. Department of Health and Human Services. Biologics. Licensing. Biologics Licensing.

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Disclaimer Information: +

Medical Policies are the Plan's guidelines for determining the medical necessity of certain services or supplies for purposes of determining coverage. These Policies may also describe when a service or supply is considered experimental or investigational, or cosmetic. In making coverage decisions, the Plan uses these guidelines and other Plan Policies, as well as the Member's benefit document, and when appropriate, coordinates with the Member's health care Providers to consider the individual Member's health care needs.

Plan Policies are developed in accordance with applicable state and federal laws and regulations, and accrediting organization standards (including NCQA). Medical Policies are also developed, as appropriate, with consideration of the medical necessity definitions in various Plan products, review of current literature, consultation with practicing Providers in the Plan's service area who are medical experts in the particular field, and adherence to FDA and other government agency policies. Applicable state or federal mandates, as well as the Member's benefit document, take precedence over these guidelines. Policies are reviewed and updated on an annual basis, or more frequently as needed. Treating providers are solely responsible for the medical advice and treatment of Members.

The use of this Policy is neither a guarantee of payment nor a final prediction of how a specific claim(s) will be adjudicated. Reimbursement is based on many factors, including member eligibility and benefits on the date of service; medical necessity; utilization management guidelines (when applicable); coordination of benefits; adherence with applicable Plan policies and procedures; clinical coding criteria; claim editing logic; and the applicable Plan – Provider agreement.