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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 04/16/2026

Kymriah™ (tisagenlecleucel)

HPCPS: Q2042

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. Prescribed by or in consultation with an oncologist
 - b. Diagnosis of pediatric and young adult with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory^a or in second or later relapse^b
 - i. FDA approved age
 - ii. Primary refractory as defined by not achieving a complete response after 2 cycles of a standard chemotherapy regimen or chemorefractory as defined by not achieving a complete response after 1 cycle of standard chemotherapy for relapsed leukemia
 - iii. Patients with Philadelphia chromosome positive (Ph+) ALL are eligible if they are intolerant to or have failed 2 lines of tyrosine kinase inhibitor therapy (TKI), or if TKI therapy is contraindicated
 - iv. Any bone marrow (BM) relapse after allogeneic stem cell transplant (SCT)
 - v. Patient must meet all of the following:
 - 1. The member has no active infection (e.g. viral, bacterial, fungal) such as HIV, active hepatitis B or active hepatitis C
 - c. Treatment of adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma:
 - i. FDA approved age
 - ii. Received ≥ 2 lines of chemotherapy, including rituximab and anthracycline
 - OR
 - iii. Relapsed following autologous hematopoietic stem cell transplantation (HSCT)
 - iv. Patient must meet all of the following:
 - 1. No known active central nervous system malignancy
 - 2. ECOG performance status 0 - 2
 - 3. Creatinine clearance greater than 30 mL/min
 - 4. Cardiac ejection fraction greater than 40%
 - 5. The member has no active infection (e.g. viral, bacterial, fungal) such as HIV, active hepatitis B or active hepatitis C
 - d. Treatment of adult patients with relapsed or refractory follicular lymphoma (FL)

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- i. Subjects must have received at least 2 prior lines of therapy
- ii. Patient must meet all of the following:
 - 1. No known active central nervous system malignancy
 - 2. ECOG performance status 0 - 2
 - 3. Creatinine clearance greater than 30 mL/min
 - 4. Cardiac ejection fraction greater than 40%
 - 5. The member has no active infection (e.g. viral, bacterial, fungal) such as HIV, active hepatitis B or active hepatitis C
- e. Have not received prior treatment with any CAR-T therapy despite indication or any other genetically-modified T-cell therapy or are being considered for treatment with any other genetically-modified T-cell therapy
- f. Only to be administered at certified bone marrow/stem cell transplant centers
- g. Trial and failure, intolerance, or a contraindication to the preferred products as listed in the BCBSM/BCN utilization management medical drug list
- h. The requesting physician attests to providing clinical outcome information within the appropriate provider portal as requested by BCBSM
- i. If new diagnoses are FDA approved, coverage will be determined based on the FDA approved indication on a case by case basis until fully evaluated by the BCBSM Pharmacy and Therapeutics Committee

B. Quantity Limitations, Authorization Period and Renewal Criteria

- a. Quantity Limits: Align with FDA recommended dosing
- b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time with the allowance of only one dose per lifetime
- c. Renewal Criteria: Not applicable as no further authorization will be provided

^a Refractory (resistant) disease is defined as those patients who fail to obtain complete response with induction therapy, ie, failure to eradicate all detectable leukemia cells (<5% blasts) from the bone marrow and blood with subsequent restoration of normal hematopoiesis (>25% marrow cellularity and normal peripheral blood counts).

^b Relapsed disease describes the reappearance of leukemia cells in the bone marrow or peripheral blood after the attainment of a complete remission with chemotherapy and/or allogeneic stem cell transplant

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- CAR-T therapy is a type of treatment that utilizes the body's own immune system to fight cancer. T-cells are collected from the patient via apheresis and are genetically engineered in the laboratory to produce chimeric antigen receptors on the cell surface, allowing the T-cells to recognize an antigen on target cancer cells. Once the tumor cells are identified, they are attacked and killed by the CAR-T therapy.
- CAR-T therapy has not been studied when given following prior treatment with any CAR-T therapy or following any other genetically-modified T-cell therapy.
- Due to the risk of cytokine release syndrome and neurological toxicities, CAR-T therapies are only allowed to be given at treatment centers certified by their REMS programs. CAR-T REMS programs require certified hospitals and

their clinics to have on-site, immediate access to tocilizumab and an understanding of how to manage the risks of the associated CAR-T side effects.

- Kymriah is indicated for patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia that is refractory or in second or later relapse. It is also approved for use in adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including DLBCL not otherwise specified, high-grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. It is not indicated for treatment of patients with primary central nervous system lymphoma.
- Safety and efficacy was established in two studies. The first was the ELIANA trial, an open-label, multicenter single-arm study of 107 pediatric and young adult patients with relapsed/refractory B-cell precursor ALL. All patients were screened, 88 were enrolled in the study, 68 were treated with CAR-T, and 63 were evaluable for efficacy. Nine percent of the enrolled subjects did not receive the product due to manufacturing failure. Treatment consisted of lymphodepleting chemotherapy (fludarabine 30 mg/m² daily for 4 days and cyclophosphamide 500 mg/m² daily for 2 days) followed by a single dose of Kymriah. Tumors must have had CD19 expressing tumor cells. Patients were included if they were primary refractory defined as not achieving a complete response after 2 cycles of a standard chemotherapy regimen or chemorefractory as defined by not achieving a complete response after 1 cycle of standard chemotherapy for relapsed leukemia; has Philadelphia chromosome positive (Ph+) ALL and were intolerant to or failed 2 lines of tyrosine kinase inhibitor therapy (TKI) or if TKI therapy was contraindicated; they were ineligible for allogeneic stem cell transplant (SCT); or had any bone marrow (BM) relapse after allogeneic SCT. Patients were excluded if they had Burkitt's lymphoma, active hepatitis B or C, any uncontrolled infection, grade 2 to 4 graft-versus-host disease, concomitant genetic syndrome with the exception of Down's syndrome, or if they have received allogeneic cellular therapy, such as donor lymphocyte infusion within 6 weeks prior to Kymriah infusion. Efficacy was based on complete remission (CR) within 3 months after infusion, the duration of CR, and proportion of patients with CR and minimal residual disease (MRD) < 0.01% by flow cytometry (MRD-negative). Among the 63 infused patients, 52 (83%) achieved CR/CRi, all of which were MRD-negative. With a median follow-up of 4.8 months from response, the median duration of CR/CRi was not reached (range: 1.2 to 14.1+ months). Median time to onset of CR/CRi was 29 days with onset of CR/CRi between 26 and 31 days for 50/52 (96%) responders. The stem cell transplantation rate among those who achieved CR/CRi was 12% (6/52).
- Efficacy was also established in the JULIET trial, an open-label, multicenter, single-arm trial of 160 adult patients with relapsed or refractory DLBCL, who received ≥ 2 lines of chemotherapy, including rituximab and anthracycline, or relapsed following autologous hematopoietic stem cell transplantation (HSCT). Of the 160 patients enrolled, 106 patients received Kymriah. Eleven patients enrolled did not receive Kymriah due to manufacturing failure and 38 other patients did not receive Kymriah due to death (n = 16), physician decision (n = 16), or adverse events (n = 3). Patients with active central nervous system malignancy, prior allogeneic HSCT, an ECOG performance status ≥ 2, a creatinine clearance < 60, alanine aminotransferase > 5 times normal, cardiac ejection fraction < 45%, or absolute lymphocyte concentration less than 300/μL were excluded from the study. The primary endpoints were complete response (CR) rate and duration of response (DOR). The median time to first response was 0.9 months (range: 0.7 to 3.3 months). The median duration of response was not reached. Response durations were longer in patients who achieved CR as compared to patients with a best response of partial response (PR). Of the 22 patients who experienced a CR, 9 achieved this status by 1 month, 12 more by month 3, and the last by month 6 after Kymriah infusion.
- Efficacy and safety were established for follicular lymphoma in the ELARA trial, a phase II, single-arm, multicenter, open-label trial of 94 adult patients with relapsed/refractory follicular lymphoma after at least two prior therapies. Patients were excluded from the study if they had active central nervous system malignancy, prior allogeneic HSCT, an ECOG performance status ≥ 2, transformed FL, or histological grade 3b FL. To be included, patients had to have measurable disease. The primary endpoint was complete response rate. The CR rate was 69% (95% CI, 60-78). Overall response rate (ORR) was 86% (95% CI, 78-92) with a 12-month progression-free survival (PFS) of 67%

(95% CI, 56-76) and nine-month DOR was 76% (95% CI, 65-84). For patients who had a complete response, 12-month PFS was 86% (95% CI, 74-92) and the estimated DOR rate was 87% (95% CI, 75-93).

- Disease should be measured/staged with PET-CT. Focal uptake in nodal and extranodal sites is considered involvement with lymphoma, including spleen, liver, bone, thyroid, and so on. A measurable node must have a longest diameter (LDi) greater than 1.5 cm. A measurable extranodal lesion should have an LDi greater than 1.0 cm. All other lesions (including nodal, extranodal, and assessable disease) should be followed as nonmeasured disease (eg, cutaneous, GI, bone, spleen, liver, kidneys, pleural or pericardial effusions, ascites).
- While use of Kymriah has not been established in patients with a creatinine clearance of less than 60 mL/minute, other CAR-T therapies have been studied in subjects with a creatinine clearance of 30 mL/minute. The National Institute of Health/National Cancer Institute Common Terminology Criteria of Adverse Events (CTCAE) classify grade 2 chronic kidney disease as a creatinine clearance of 30 – 59 mL/minute. As the classification system uses 30 mL/minute as a cutoff for grade 2 disease and data from other CAR-T therapies support their use in these patients, Kymriah should be able to be tolerated in this population. As there is no data to support administration of CAR-T at levels lower than 30 ml/minute, therapy should not be given in patients not meeting the 30 mL/minute threshold.
- The CTCAE recommendations set the grade 2 cutoff for left ventricular ejection fraction (LVEF) at 40%. While Kymriah has only been studied in patients with a LVEF greater than or equal to 45%, there is data from other CAR-T therapies to support use in those with a LVEF of 40% or greater. Therefore, Kymriah should be tolerated in these patients as well. There is no data supporting use at LVEF levels less than 40%.
- A provider portal that is used to capture clinical outcome information for patients on select high-cost treatments, such as gene and cellular therapies. If a patient meets medical necessity as defined by this policy and is approved for treatment, the requesting physician must attest to providing clinical outcome information within the appropriate provider portal at the requested cadence.

References:

1. Kymriah [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2025.
2. Clinicaltrials.gov. A phase II, single arm, multicenter trial to determine the efficacy and safety of CTL019 in pediatric patients with relapsed and refractory b-cell acute lymphoblastic leukemia. Available at: <https://clinicaltrials.gov/ct2/show/study/NCT02435849>. Accessed on August 3, 2017.
3. LaRussa A. Chimeric antigen receptor (CAR) t-cell therapy. 10 Sept. 2015. Available at: www.lls.org/treatment/types-of-treatment/immunotherapy/chimeric-antigen-receptor-car-t-cell-therapy. Access on August 3, 2017.
4. National Comprehensive Cancer Network. Pediatric acute lymphoblastic leukemia (Version 1.2026). 2025 August 11. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed on March 3, 2026.
5. National Comprehensive Cancer Network. Acute lymphoblastic leukemia (Version 2.2025). 2025 June 27. Available at: https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed on March 3, 2026.
6. National Comprehensive Cancer Network. B-cell lymphomas (Version 2.2026). 2026 March 2. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed on March 3, 2026.
7. Lee DW et al. Current concepts in the diagnosis and management of cytokine release syndrome. *Blood*. 2014 Jul 10; 124 (2): 188 - 195.
8. Clinicaltrials.gov. A phase II, single arm, multicenter trial to determine the efficacy and safety of CTL019 in adult patients with relapsed or refractory diffuse large b-cell lymphoma (DLBCL). Available at: <https://clinicaltrials.gov/ct2/show/NCT02445248>. Accessed on August 3, 2017.
9. Clinicaltrials.gov. A phase II, single arm, multicenter open label trial to determine the efficacy and safety of tisagenlecleucel (CTL019) in adult patients with refractory or relapsed follicular lymphoma (NCT03568461). Available at:

<https://clinicaltrials.gov/ct2/show/NCT03568461?cond=follicular+lymphoma&intr=%22Kymriah%22+OR+%22Tisagen%22+OR+%22CTL019%22&draw=2&rank=1>. Accessed on March 9, 2022.

10. U.S. Department of Health and Human Services. Common terminology criteria for adverse events (Version 5.0). 2017 Nov 27. Available at: https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_8.5x11.pdf. Accessed on July 6, 2022.

Policy History												
#	Date	Change Description										
1.9	Effective Date: 04/16/2026	Updated to remove no prior allogenic stem cell transplant, lymphocyte counts, liver function test, no HIV, hepatitis C or B infection, no uncontrollable infection or infection requiring long term antibiotics, no significant cardiac events, no thromboemolic events within 6 months, no pulmonary disease, no clinically significant CNS disease, no measureable FL, no transformed FL, and no grade 3b FL. Also added requirements of no active infection and updated the approval length to 6 months										
1.8	Effective Date: 06/05/2025	Updated to change the provider portal from Audaire Health to the appropriate provider portal										
1.7	Effective Date: 06/06/2024	Annual review of criteria was performed, no changes were made										
1.6	Effective Date: 06/08/2023	Updated to require physicians to provide clinical outcomes data using the Audaire Health platform										
1.5	Effective Date: 08/04/2022	Updated to align criteria across all CAR-T policies and include new indication for use in relapsed/refractory FL										
1.4	Effective Date: 04/14/2022	Updated to remove CD19 requirement as NCCN guidelines state CAR-T can work without being positivefor CD19 disease and add preliminary criteria for use in relapsed/refractory FL										
1.3	Effective Date: 08/12/2021	New policy - this policy replaces previously approved criteria that was embedded in Chimeric Antigen Receptor-T Cell Class policy which will be retired										
1.2	Effective Date: 03/08/2018	UM medical management system update for BCNA and MAPPO <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
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1.1	Effective Date: 12/01/2017	UM medical management system update for BCBS <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	No	BCNA	No
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1.0	Effective Date: 11/09/2017	UM medical management system update for BCN										
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BCN	Yes											
MAPPO	No											
BCNA	No											

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.*

Blue Cross Blue Shield/Blue Care Network of Michigan

Medication Authorization Request Form



This form is to be used by participating physicians to obtain coverage for **drugs covered under the medical benefit**. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

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PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	Name
ID Number	Specialty
D.O.B. ☐ Male ☐ Female	Address
Diagnosis	City /State/Zip
Drug Name	Phone/Fax: P: () - F: () -
Dose and Quantity	NPI
Directions	Contact Person
Date of Service(s)	Contact Person Phone / Ext.

STEP 1: DISEASE STATE INFORMATION

- Is this request for: ☐ Initiation ☐ Continuation Date patient started therapy: _____
- Administered by patient or a medical professional? ☐ patient (self) ☐ health care professional (physician, nurse, etc.)
- Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
☐ Hospital outpatient facility (go to #4) Reason for Hospital Outpatient administration: _____
☐ Hospital inpatient facility for Car-T therapy only (for example: Kymriah, Yescarta, or Tecartus) (go to #5)
- Please specify location of administration if hospital outpatient infusion: _____
- Please specify location of administration if hospital inpatient infusion: _____
- Please provide the NPI number for the place of administration: _____
- Initiation AND Continuation of therapy:**
 - What is the patient's diagnosis? _____
 - What other medication has the patient received for their condition? Please list _____
 - Please describe the response to previous therapies: _____
 - Will the patient be receiving any other treatment for the listed condition while on this medication? Please list: _____
 - Please list any labs values important for diagnosing or monitoring this patient's condition: _____
- Continuation of therapy:**
 - Has the patient progressed while on this medication? ☐ yes ☐ no
 - How has the patient's condition changed while on this medication?

☐ Improved: Please describe: _____
 ☐ Stable: please describe: _____
 ☐ Worsened; Please describe: _____
 ☐ Other; Please describe: _____

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review (required)

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
Step 2: Checklist	☐ Form Completely Filled Out ☐ Provide chart notes	☐ Attach test results
Step 3: Submit	By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979	By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320

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7/26/2018, 9/18/2018; 1/31/2020; 3/17/2020; 8/9/2021