Medical Policy

Kymriah® (tisagenlecleucel)	
MEDICAL POLICY NUMBER	MED_Clin_Ops_030
CURRENT VERSION EFFECTIVE DATE	January 1, 2024
APPLICABLE PRODUCT AND MARKET	*Individual Family Plan:* All Plans *Small Group*: All Plans *Medicare Advantage:* All Plans

Brand New Day/Central Health Medicare Plan develops policies and makes coverage determinations using credible scientific evidence including but not limited to MCG™ Health Guidelines, the ASAM Criteria™, and other third party sources, such as peer-reviewed medical literature generally recognized by the relevant medical community, physician specialty society recommendations, and expert opinion as relevant to supplement those sources. Brand New Day/Central Health Medicare Plan Medical Policies, MCG™ Guidelines, and the ASAM Criteria™ are not intended to be used without the independent clinical judgment of a qualified health care provider considering the individual circumstances of each member's case. The treating health care providers are solely responsible for diagnosis, treatment, and medical advice. Members may contact Brand New Day/Central Health Medicare Plan Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions about this Brand New Day/ Central Health Medicare Plan policy may contact the Health Plan. Brand New Day/Central Health Medicare Plan policies and practices are compliant with federal and state requirements, including mental health parity laws.

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PURPOSE

To promote consistency between reviewers in clinical coverage decision-making by providing the criteria that generally determine the medical necessity of Kymriah® (tisagenlecleucel) therapy

POLICY/CRITERA
Prior Authorization and Medical Review is required.

Coverage of Kymriah® (tisagenlecleucel) is approved for patients with a diagnosis of B-cell precursor acute lymphoblastic leukemia (ALL) when all the below criteria are met:

1. Patient is between the ages of 3 and 25 years of age at the time of treatment; **AND**
2. Patient has a confirmed diagnosis of B-cell precursor ALL; **AND**
3. Patient has confirmed CD 19-positive disease; **AND**
4. Patient's disease is refractory or in a second of later relapse defined by one of the following:
    a. Second or greater bone marrow (BM) relapse; **OR**
    b. Any BM relapse after allogenic stem cell transplantation (SCT); **OR**

   c. Patient has been treated with 2 cycles of standard chemotherapy and has not achieved complete response; **OR**
   d. Patient experienced a relapse, was treated with 1 cycle of standard chemotherapy and has not achieved complete response; **OR**
   e. If Patient has Philadelphia chromosome (Ph)-positive disease has a contraindication to, is intolerant to, or has failed two lines of tyrosine kinase inhibitor (TKI) therapy; **AND**
5. Patient has a life expectancy greater than 12 weeks; **AND**
6. Patient has a performance status (Karnofsky or Lansky) greater than 50%; **AND**
7. Patient is not currently pregnancy; **AND**
8. If patient is a sexually active female of reproductive potential, a negative pregnancy test is documented; **AND**
9. Patient does not have a clinically significant active infection or inflammatory disorder; **AND**
10. Patient has not received live vaccines within 2 weeks prior to the start of lymphodepleting chemotherapy, during Kymriah treatment, and will not receive live vaccines until immune recovery following treatment; **AND**
11. Patient has been screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines prior to collection of cells (leukapheresis); **AND**
12. Prophylaxis for infection has been followed according to local guidelines **AND**
13. Patient will be using Kymriah in conjunction with lymphodepleting chemotherapy (fludarabine 30 mg/m2 intravenously daily for 4 days and cyclophosphamide 500 mg/m2 intravenously for 2 days starting with the first dose of fludarabine); **AND**
14. Kymriah will be infused 2 to 14 days after completion of lymphodepleting chemotherapy; **AND**
15. Patient will be premedicated with acetaminophen and diphenhydramine (or another H1-antihistamine) 30 to 60 minutes prior to infusion of Kymriah; **AND**
16. Tocilizumab and emergency equipment are available prior to infusion of Kymriah and during the recovery period; **AND**
17. The requesting provider belongs to a healthcare facility that has enrolled in the Kymriah REMS program and training has been given to providers on the management of cytokine release syndrome (CRS) and neurological toxicities; **AND**
18. Kymriah infusion will occur at a treatment center that is certified to administer Kymriah; **AND**
19. Patient will be monitored for signs and symptoms of Cytokine Release Syndrome (CRS) for at least 4 weeks after treatment with Kymriah and will be counselled to seek immediate medical attention should signs and symptoms of CRS or a neurological event occur at any time; **AND**
20. Patient will stay within proximity (within 2 hours) of the Kymriah treatment site for at least 4 weeks following infusion.

Coverage of Kymriah® (tisagenlecleucel) is approved for patients with a diagnosis of relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy when all the following criteria are met:

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1. Patient is 18 years of age or older; **AND**
2. Patient has a confirmed diagnosis of relapsed or refractory large B-cell lymphoma, including:
    a. Diffuse large B-cell lymphoma (DLBCL) not otherwise specified; **OR**
    b. High grade B-cell lymphoma; **OR**
    c. DLBCL arising from follicular lymphoma; **AND**
3. Patient's disease is relapsed or refractory, as defined as:
    a. Having received 2 or more lines of chemotherapy, including rituximab and anthracycline; **OR**
    b. Having relapsed following autologous hematopoietic stem cell transplantation (HSCT); **AND**
4. Patient has confirmed CD 19-positive disease; **AND**
5. Patient has an ECOG performance score ≤ 1; **AND**
6. Patient has a creatinine clearance ≥ 60; **AND**
7. Patient's alanine aminotransferase ≤ 5 times normal; **AND**
8. Patient's cardiac ejection fraction ≥ 45%; **AND**
9. Patient's absolute lymphocyte concentration is ≥ 300/µL; **AND**
10. Patient is not currently pregnant; **AND**
11. If Patient is a sexually active female of reproductive potential, confirm they have had their pregnancy status verified through a pregnancy test; **AND**
12. Patient does not have a clinically significant active infection or inflammatory disorder; **AND**
13. Patient has not received live vaccines within 2 weeks prior to the start of lymphodepleting chemotherapy, during Kymriah treatment, and will not receive live vaccines until immune recovery following treatment; **AND**
14. Patient has been screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines prior to collection of cells (leukapheresis); **AND**
15. Prophylaxis for infection has been followed according to local guidelines; **AND**
16. Patient will be using Kymriah in conjunction with one of the following lymphodepleting chemotherapy regimens:
    a. Fludarabine (25 mg/m2 i.v. daily for 3 days) and cyclophosphamide (250 mg/m2 IV daily for 3 days starting with the first dose of fludarabine; **OR**
    b. Bendamustine 90 mg/m2 i.v. daily for 2 days if a patient experienced a previous Grade 4 hemorrhagic cystitis with cyclophosphamide or demonstrates resistance to a previous cyclophosphamide containing regimen; **OR**
    c. Lymphodepleting chemotherapy will be omitted due to white blood cell (WBC) count less than or equal to 1 x 109/L within 1 week prior to Kymriah; **AND**
17. Kymriah will be infused 2 to 11 days after completion of lymphodepleting chemotherapy, or within 1 week if lymphodepleting chemotherapy is to be omitted; **AND**
18. Patient will be premedicated with acetaminophen and diphenhydramine (or another H1-antihistamine) 30 to 60 minutes prior to infusion of Kymriah; **AND**
19. Tocilizumab and emergency equipment are available prior to infusion of Kymriah and during the recovery period; **AND**

20. The requesting provider belongs to a healthcare facility that has enrolled in the Kymriah REMS program and training has been given to providers on the management of cytokine release syndrome (CRS) and neurological toxicities; **AND**
21. Kymriah infusion will occur at a treatment center that is certified to administer Kymriah; **AND**
22. Patient will be monitored for signs and symptoms of Cytokine Release Syndrome (CRS) for at least 4 weeks after treatment with Kymriah and will be counselled to seek immediate medical attention should signs and symptoms of CRS or a neurological event occur at any time; **AND**
23. Patient will stay within proximity (within 2 hours) of the Kymriah treatment site for at least 4 weeks following infusion.

LIMITATIONS/EXCLUSIONS

1. Approval will be granted for 1 single dose of Kymriah
2. Coverage cannot be renewed; a maximum of 1 dose per lifetime will apply
3. Patient must not have previously received CAR-T or other gene therapy
4. Patient must not have a diagnosis of Burkitt's lymphoma/leukemia or a concomitant genetic syndrome (e.g., Fanconi anemia, Kostmann syndrome, Shwachman syndrome, or any other known bone marrow failure syndrome)
5. Kymriah is not indicated for the treatment of patients with a primary central nervous system lymphoma

BACKGROUND

Kymriah® (tisagenlecleucel) is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse and adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

DEFINITIONS

1. Kymriah Suspension for intravenous infusion. Initial Approval: August 30, 2017.
    a. Kymriah is a suspension for intravenous infusion, supplied as single patient-specific infusion bag containing up to 2.5 x 10^6 CAR-positive T Cells
    b. Kymriah is dosed according to indication and patient weight reported at time of leukapheresis:
        i. Pediatric and young adult B-cell ALL
            1. Patients ≤ 50 kg: 0.2 to 5.0 x 10^6 CAR-positive T cells per kg of body weight
            2. Patients > 50 kg: 0.1 to 2.5 x 10^8 CAR-positive viable T cells
        ii. Adult relapsed or refractory diffuse large B-cell lymphoma
            1. 0.6 to 6.0 x 10^8 CAR-positive viable T cells

CODING

Applicable NDC Codes	
00078-0846-19	00078-0958-19

Applicable Procedure Code	
Q2042	Tisagenlecleucel, up to 250 million CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per infusion

Applicable ICD-10 Codes	
C83.30	Diffuse large B-cell lymphoma, unspecified site
C83.31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.32	Diffuse large B-cell lymphoma, intrathoracic lymph nodes
C83.33	Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
C83.34	Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
C83.35	Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.36	Diffuse large B-cell lymphoma, intrapelvic lymph nodes
C83.37	Diffuse large B-cell lymphoma, spleen
C83.38	Diffuse large B-cell lymphoma, lymph nodes of multiple site
C83.39	Diffuse large B-cell lymphoma, extranodal and solid organ sites
C91.00	Acute myeloblastic leukemia, not having achieved remission
C91.02	Acute myeloblastic leukemia, in relapse
Z51.12	Encounter for antineoplastic immunotherapy

EVIDENCE BASED REFERENCES

1. Kymriah [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corp., May 2018. Accessed December 2019
2. Grupp S, Laetsch T, Buechner J, et al. Analysis of a global registration trial of the efficacy and safety of CTL019 in pediatric and young Adults with relapsed/refractory acute lymphoblastic leukemia (ALL). Blood. 2016; 128(22):221.
3. Novartis (2018). Risk Evaluation and Mitigation Strategy (REMS): Cytokine Release Syndrome and Neurological Toxicities [PowerPoint slides] Available at: http://www.kymriah-rems.com/globalassets/kymriah-rems3/kym-1180086-kymriahremslivetrainingprogram.pdf Accessed April 2018.
4. Porter DL, Hwang WT, Frey NV, et al. Chimeric antigen receptor T cells persist and induce sustained remissions in relapsed refractory chronic lymphocytic leukemia. Sci Transl Med. 2015 Sep 2;7(303):303ra139. doi: 10.1126/scitranslmed.aac5415.

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POLICY HISTORY

Original Effective Date	December 7, 2020
Revised Date	November 1, 2021 – Annual Review and approval (no policy revisions made) February 2, 2022 – Annual Review and approval (no policy revisions made) March 1, 2023 – Adopted by MA UM Committee (no policy revisions made) January 1, 2024 - Updated to Brand New Day/Central Health Medicare Plan (no policy revisions made)

Approved by Pharmacy and Therapeutics Committee on 2/2/2022