Drug Policy:

Kymriah™ (tisagenlecleucel)

POLICY NUMBER UM ONC_1324	**SUBJECT** Kymriah™ (tisagenlecleucel)		**DEPT/PROGRAM** UM Dept	**PAGE 1 of 4**
DATES COMMITTEE REVIEWED 09/13/17, 09/21/18, 08/14/19, 12/11/19, 06/10/20, 02/10/21, 05/12/21, 11/15/21, 02/09/22	**APPROVAL DATE** February 9, 2022	**EFFECTIVE DATE** February 25 2022	**COMMITTEE APPROVAL DATES** 09/13/17, 09/21/18, 08/14/19, 12/11/19, 06/10/20, 02/10/21, 05/12/21, 11/15/21, 02/09/22	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS HUM 1	**NCQA STANDARDS** UM 2		**ADDITIONAL AREAS OF IMPACT**	
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Kymriah (tisagenlecleucel) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

New Century Health (NCH) is responsible for processing all medication requests from network ordering providers. Medications not authorized by NCH may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

1. When health plan Medicaid coverage provisions—including any applicable PDLs (Preferred Drug Lists)—conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the Preferred Drug Guidelines OR
2. When health plan Exchange coverage provisions-including any applicable PDLs (Preferred Drug Lists)-conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the Preferred Drug Guidelines OR

3. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the Preferred Drug Guidelines shall follow NCH L1 Pathways when applicable, otherwise shall follow NCH drug policies AND
4. Continuation requests of previously approved, non-preferred medication are not subject to this provision AND
5. When applicable, generic alternatives are preferred over brand-name drugs.

B. Acute Lymphoblastic Leukemia (ALL)

1. Kymriah (tisagenlecleucel) is being used when the following criteria are met:
    a. Member is 25 years old or younger, and has Acute Lymphoblastic Leukemia with confirmed documentation of CD19 tumor expression (demonstrated in bone marrow or peripheral blood by flow cytometry) AND
    b. Member has experienced disease relapse after allogeneic stem cell transplantation (SCT) and member is ≥ 6 months from above transplantation at the time of infusion OR
    c. Member has relapsed/refractory Philadelphia chromosome-negative B-ALL that has progressed after 2 cycles of a standard chemotherapy regimen for initial diagnosis OR after 1 cycle of standard chemotherapy for relapsed leukemia OR
    d. Member has relapsed/refractory Philadelphia chromosome-positive B-ALL that has progressed after failure of 2 prior regimens, including a TKI-containing regimen with Gleevec (imatinib), Bosulif (bosutinib), Sprycel (dasatinib), Tasigna (nilotinib), or Iclusig (ponatinib).

C. B-Cell Lymphomas

1. Kymriah (tisagenlecleucel) may be used for members who are 18 years of age or older, with Diffuse Large B-Cell Lymphoma, transformed Follicular Lymphoma, high-grade B-cell lymphoma with MYC rearrangement plus rearrangement of BCL2, BCL6, or both genes (i.e., double- or triple-hit lymphoma) with confirmed documentation of CD19 tumor expression. AND
2. Members must have previously received at least two lines of therapy, including rituximab and an anthracycline, unless anthracyclines are contraindicated (for DBCL) AND
3. Either having failed autologous Hematopoietic stem cell transplantation (ASCT) or being ineligible for or not consenting to ASCT.

III. EXCLUSION CRITERIA

A. Kymriah (tisagenlecleucel) is being used after disease progression on or after CAR-T cell therapy directed towards CD19 antigen [Kymriah ((tisagenlecleucel), Breyanzi (lisocabtagene maraleucel), or Yescarta (axicabtagene ciloleucel].

B. Member does not have adequate bone marrow reserve defined by **ALL** of the following:
    1. Absolute neutrophil count (ANC) ≥ 1000/uL
    2. Platelet Count ≥ 50,000/uL

C. Member does not have adequate renal, hepatic, cardiac and pulmonary function defined as:
    1. Creatinine clearance ≥ 60 mL/min
    2. Serum ALT ≤5 times the upper limit of normal
    3. Cardiac ejection fraction ≥ 45%, no evidence of pericardial effusion as determined by an echocardiogram (ECHO), and no clinically significant pleural effusion.

D. History of seizures or other CNS disorder.

E. History of autoimmune disease.

F. Active serious infection.

G. Previous allogeneic transplant.

H. Active CNS involvement with lymphoma.

I. Dosing exceeds single dose limit of Kymriah (tisagenlecleucel) 0.6 to 6.0 x 10^8 CAR-positive viable T cells (for B-Cell Lymphomas); 0.1 to 2.5 x 10^8 CAR-positive viable T cells (for ALL).

J. Does not exceed duration limit as one time administration.

K. Investigational use of Kymriah (tisagenlecleucel) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of < 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

A. Schuster SJ, et al. JULIET Trial. Tisagenlecleucel in Adult Relapsed or Refractory Diffuse Large B-Cell Lymphoma. N Engl J Med. 2019 Jan 3;380(1):45-56.

B. Maude SL, et al. CART19 Trial. Chimeric antigen receptor T cells for sustained remissions in leukemia. N Engl J Med. 2014 Oct 16;371(16):1507-17.

C. Kymriah prescribing information. Novartis Pharmaceuticals Corporation. East Hanover, NJ 2021.

D. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.

E. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.