Molina Clinical Policy
Kymriah™ (tisagenlecleucel)
Policy Number: 395

Last Approval: 6/14/2023
Next Review Due By: June 2024

POLICY SECTIONS

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

POLICY DESCRIPTION

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

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.

RELATED POLICIES

Policy No.	Policy Title
N/A	

INDICATIONS and/or LIMITATIONS OF COVERAGE

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 (http://pathways.newcenturyhealth.com/) 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; **AND**
6. When there is a documented drug shortage, disease progression, contraindication, or confirmed intolerance to a Preferred drug/regimen, per NCH Policy and Pathway, the available alternative product may be used if deemed medically appropriate and the indication is listed in a standard reference compendia or accepted peer review literature. For a list of current drug shortages, please refer to FDA drug shortage website in the reference section.

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 B- Cell ALL that has progressed after 2 lines of a standard chemotherapy regimen with or without a TKI; use with a TKI [e.g., Gleevec (imatinib)] is for members with Philadelphia chromosome-positive B-Cell ALL

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**
   a. Members must have previously received at least two lines of therapy, including rituximab and an anthracycline, unless anthracyclines are contraindicated (for DBCL); **AND**
   b. Either having failed autologous Hematopoietic stem cell transplantation (ASCT) or being ineligible for or not consenting to ASCT.

   OR
2. Kymriah (tisagenlecleucel) may be used in adult members with confirmed documentation of CD19 positive relapsed or refractory follicular lymphoma (Grade 1, 2, 3A) after 2 or more lines of systemic therapy, failure to maintenance therapy following at least two lines of therapy, and/or have failed autologous Hematopoietic stem cell transplantation (ASCT). For the above prior lines of therapy, these include chemoimmunotherapy with an anti-CD20 agent AND an alkylating agent (e.g., rituximab/obinutuzumab + bendamustine, rituximab/obinutuzumab + CHOP, rituxumab/obinutuzumab + CVP).

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. CD-19 positivity not confirmed and documented.

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) 6.0 x 10^8 CAR-positive viable T cells (for B-Cell Lymphomas); 2.5 x 10^8 CAR-positive viable T cells (for ALL).

J. Exceeds 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.

MEDICATION MANAGEMENT

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

ATTACHMENTS

NONE

APPLICABLE CPT / HCPCS PROCEDURE CODES

CPT (Current Procedural Terminology) Codes

CPT	Description
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 (eg, 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 (Healthcare Common Procedure Coding System) Code

HCPCS	Description
Q2042	Tisagenlecleucel, up to 600 million CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose

AVAILABLE DOSAGE FORMS: Single-dose unit infusion bag: frozen suspension of genetically modified autologous T cells labeled for the specific recipient

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

6/14/2023 Policy revision to include members with relapsed/refractory ALL progressed after 2 lines of standard chemotherapy and added exclusion criteria-must have documented CD19. Removed codes C9399, J3490, J3590, and J9999.
8/10/2022 Adopted NCH policy and retired MCP.

REFERENCES

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