Evolent Clinical Guideline 3012 for Kymriah™ (tisagenlecleucel)

Guideline Number:	Applicable Codes	
Evolent_CG_3012		
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Original Date:	**Last Revised Date:**	**Implementation Date:**
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STATEMENT

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.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent 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.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Acute Lymphoblastic Leukemia (ALL)

- Kymriah (tisagenlecleucel) may be used in members up to 25 years of age with B-cell ALL that is refractory or in second or later relapse.

B-Cell Lymphomas

- Kymriah (tisagenlecleucel) may be used for adult members 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.

Follicular Lymphoma

- Kymriah (tisagenlecleucel) may be used for adult members with relapsed or refractory follicular lymphoma after two or more lines of systemic therapy.

CONTRAINDICATIONS/WARNINGS

- US Boxed Warning
    - Cytokine release syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving tisagenlecleucel. Do not administer tisagenlecleucel to patients with active infection or inflammatory disorders. Treat

severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.

- Neurological toxicities, including severe or life-threatening reactions, occurred following treatment with tisagenlecleucel, including concurrently with CRS. Monitor for neurological events after treatment with tisagenlecleucel. Provide supportive care and/or corticosteroids as needed.
- T cell malignancies have occurred following treatment of hematologic malignancies with BCMA- and CD19-directed genetically modified autologous T cell immunotherapies, including tisagenlecleucel.

EXCLUSION CRITERIA

- Kymriah (tisagenlecleucel) is being used after disease progression on or after the same regimen or another CAR-T cell therapy directed towards CD19 antigen [Breyanzi (lisocabtagene maraleucel), Tecartus (brexucabtagene autoleucel), or Yescarta (axicabtagene ciloleucel)].
- CD-19 positivity not confirmed and documented.
- Active CNS involvement with lymphoma.
- 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).
- Does not exceed duration limit as one time administration.
- 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:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - 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 less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
  - Whether the experimental design, considering 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).
  - 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.
  - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for

determining accepted uses of drugs.

- 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.

CODING AND STANDARDS

Codes

- Q2042 - Tisagenlecleucel, up to 600 million car-positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
February 2026	• Updated contraindications/warnings section • Updated references
February 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1324 Kymriah (tisagenlecleucel) • Added "Follicular Lymphoma" to indications section
February 2024	• Updated indication section to follow FDA labeling • Updated exclusion criteria • Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Services Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

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