Molina Clinical Policy
Yescarta™ (axicabtagene ciloleucel)
Policy Number: 396

Last Approval: 8/9/2023
Next Review Due By: August 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 Yescarta (axicabtagene ciloleucel) 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.

INDICATIONS and/or LIMITATIONS OF COVERAGE

A. Continuation requests for a not-approvable medication shall be exempt from this policy provided:

1. The requested medication was used within the last year; **AND**
2. The member has not experienced disease progression and/or no intolerance to the requested medication; **AND**
3. Additional medication(s) are not being added to the continuation request.

B. Non-Hodgkin Lymphomas (NHL), Confirmed CD-19 Positive

1. The member has **ONE** of the following aggressive, CD-19 positive NHL:
   a. Diffuse Large B Cell Lymphoma (DLBC) **OR**
   b. Primary Mediastinal Large B Cell Lymphoma (PMBCL) **OR**
   c. Transformed Follicular Lymphoma (TFL) (transformed to Diffuse Large B-Cell or other high-grade lymphoma) **OR**
   d. High-grade B-cell lymphomas with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma) or high-grade B-cell lymphomas, not otherwise specified **OR**

e. Monomorphic post-transplant lymphoproliferative disorders (B-cell type).

AND

2. The member has chemotherapy-refractory disease after the following:
   a. Two or more lines of systemic chemotherapy **OR**
   b. First line chemoimmunotherapy or relapses within 12 months of first line systemic chemotherapy, including rituximab and an anthracycline (e.g., R-CHOP, R-CEOP, R- EPOCH).

C. Follicular Lymphoma (FL), Confirmed CD-19 Positive

1. Yescarta (axicabtagene ciloleucel) may be used in adult members with CD19 positive relapsed or refractory follicular lymphoma (FL) who have received and experienced disease progression on two or more lines of systemic therapies, including the combination of an anti- CD20 monoclonal antibody and an alkylating agent (e.g., rituximab/obinutuzumab + bendamustine, rituximab/obinutuzumab + CHOP, rituxumab/obinutuzumab + CVP).

EXCLUSION CRITERIA

A. Yescarta (axicabtagene ciloleucel) is being used after disease progression with the same regimen or prior CAR-T cell therapy directed towards CD19 antigen [e.g., Kymriah (tisagenlecleucel), Breyanzi (lisocabtagene maraleucel), or Tecartus (brexucabtagene autoleucel)].

B. Concurrent use with other systemic immunosuppressive therapy or live virus vaccines.

C. Lack of confirmed CD-19 positivity in lymphoma cells.

D. Treatment exceeds the maximum duration limit as one time administration.

E. Treatment with Yescarta (axicabtagene ciloleucel) exceeds the maximum limit of 2 × 108 CAR-positive viable T cells per kg body weight.

F. The member does not have adequate bone marrow reserve defined by **ALL** of the following:

1. Absolute neutrophil count (ANC) ≥ 1000/Ul
2. Platelet Count ≥ 75,000/uL.

G. The member does not have adequate renal, hepatic, cardiac and pulmonary function defined as:

1. Creatinine clearance ≥ 60 mL/min
2. Serum ALT/AST <2.5 times the upper limit of normal
3. Total bilirubin <1.5 mg/dl, except in subjects with Gilbert's syndrome
4. Cardiac ejection fraction ≥ 50%, no evidence of pericardial effusion as determined by an echocardiogram (ECHO), and no clinically significant pleural effusion.

H. Investigational use of Yescarta (axicabtagene ciloleucel) 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, 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).
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

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

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
Q2041	Axicabtagene Ciloleucel, up to 200 million autologous Anti-CD19 CAR T Cells, including leukapheresis and dose preparation procedures, per infusion

AVAILABLE DOSAGE FORMS: A suspension for intravenous infusion. Each single infusion bag of Yescarta contains a suspension of CAR-positive T cells in approximately 68 mL.

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

8/09/2023	Changes to indications/inclusion criteria to remove reference to preferred drug listing and deleted multiple existing exclusionary criteria. Reviewed by board certified Oncologist.
8/10/2022	Adopted NCH policy and retired MCP.

REFERENCES

A. Locke FL, et al. ZUMA-7 Clinical Trial. Axicabtagene Ciloleucel as Second-Line Therapy for Large B-Cell Lymphoma. N Engl J Med. 2022 Feb 17;386(7):640-654.
B. Neelapu SS, et al. ZUMA-1 Clinical Trial. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. N Engl J Med. 2017 Dec 28;377(26):2531-2544.
C. Richardson C, et al. Primary Analysis of Zuma-5: A Phase 2 Study of Axicabtagene Ciloleucel (Axi-Cel) in Patients with Relapsed/Refractory (R/R) Indolent Non-Hodgkin Lymphoma (iNHL). Blood 2020; 136 (Supplement 1):40-41.
D. Yescarta prescribing information. Kite Pharma, Inc. Santa Monica, CA 2022.
E. 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.
F. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf
G. NCQA UM 2023 Standards and Elements.