New Century Health

Drug Policy:

Yescarta™ (axicabtagene ciloleucel)

POLICY NUMBER UM ONC_1329	SUBJECT Yescarta™ (axicabtagene ciloleucel)		DEPT/PROGRAM UM Dept	PAGE 1 of 4
DATES COMMITTEE REVIEWED 11/08/17, 10/10/18, 10/09/19, 12/11/19, 06/10/20, 02/10/21, 04/14/21, 05/12/21, 11/15/21, 02/09/22, 05/11/22, 06/08/22, 09/14/22, 07/12/23	APPROVAL DATE July 12, 2023	EFFECTIVE DATE July 28, 2023	COMMITTEE APPROVAL DATES 11/08/17, 10/10/18, 10/09/19, 12/11/19, 06/10/20, 02/10/21, 04/14/21, 05/12/21, 11/15/21, 02/09/22, 05/11/22, 06/08/22, 09/14/22, 07/12/23	
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
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 Yescarta (axicabtagene ciloleucel) 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. Continuation requests for a not-approvable medication shall be exempt from this NCH 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. 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, rituximab/obinutuzumab + CVP).

C. 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 (DLBCL)
   b. Primary Mediastinal Large B Cell Lymphoma (PMBCL)
   c. Transformed Follicular Lymphoma (TFL) (transformed to Diffuse Large B-Cell or other high grade lymphoma)
   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
   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).

III. EXCLUSION CRITERIA

A. Yescarta (axicabtagene ciloleucel) is being used on or 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 of other systemic immunosuppressive therapy or live virus vaccines.

C. Lack of confirmed documentation of 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 2×10^8 CAR-positive viable T cells per kg body weight, up to a maximum total dose of 2×10^8 CAR-positive viable T cells.

F. The member does not have adequate bone marrow reserve defined by ALL of the following:
   1. Absolute neutrophil count (ANC) greater than or equal to 1000/uL
   2. Platelet Count greater than or equal to 75,000/uL.

G. The member does not have adequate renal, hepatic, cardiac and pulmonary function defined as:
   1. Creatinine clearance greater than or equal to 60 mL/min
   2. Serum ALT/AST less than 2.5 times the upper limit of normal
   3. Total bilirubin less than 1.5 mg/dl, except in subjects with Gilbert's syndrome
   4. Cardiac ejection fraction greater than or equal to 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 definitions 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.
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.

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. 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.