Drug Policy:

Adakveo™ (crizanlizumab)

POLICY NUMBER UM ONC_1375	**SUBJECT** Adakveo™ (crizanlizumab)		**DEPT/PROGRAM** UM Dept	**PAGE 1 OF 3**
DATES COMMITTEE REVIEWED 12/11/19, 10/14/20, 03/10/21, 11/15/21, 03/09/22, 05/11/22, 02/08/23, 02/14/24	**APPROVAL DATE** February 14, 2024	**EFFECTIVE DATE** February 23, 2024	**COMMITTEE APPROVAL DATES** 12/11/19, 10/14/20, 03/10/21, 11/15/21, 03/09/22, 05/11/22, 02/08/23, 02/14/24	
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, Medicare	

I. PURPOSE

To define and describe the accepted indications for Adakveo (crizanlizumab) 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.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

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

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

B. Sickle Cell Disease

1. Adakveo (crizanlizumab) may be used in members aged 16-65 years with ALL the following:
   a. Sickle cell disease (HbSS, HbSC, HbS/beta0-thalassemia, HbS/beta+-thalassemia, and other less common genotypes) AND
   b. Two or more sickle cell-related pain crises in the past 12 months AND

c. If receiving Hydroxyurea, treatment must be prescribed for at least 6 months AND on a stable dose of Hydroxyurea for at least 3 months.

III. EXCLUSION CRITERIA

A. Adakveo (crizanlizumab) is being used after disease progression with the same regimen.

B. Receiving chronic anticoagulation therapy (e.g., warfarin, heparin) other than aspirin.

C. The member has a hemoglobin level less than 4.0 g/dL.

D. Dosing exceeds single dose limit of Adakveo (crizanlizumab) 5 mg/kg.

E. Investigational use of Adakveo (crizanlizumab) 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. Ataga KI, et al. SUSTAIN Clinical Trial. Crizanlizumab for the Prevention of Pain Crises in Sickle Cell Disease. N Engl J Med. 2017 Feb 2;376(5):429-439.

B. Adakveo prescribing information. Novartis Pharmaceuticals Corporation. East Hanover, New Jersey 2022.

C. Clinical Pharmacology Elsevier Gold Standard 2023.

D. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.

E. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.

F. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.

G. 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.

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

I. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.