

Drug Policy:

Brukinsa™ (zanubrutinib)

POLICY NUMBER UM ONC_1377	SUBJECT Brukinsa™ (zanubrutinib)		DEPT/PROGRAM UM Dept	PAGE 1 of 3
DATES COMMITTEE REVIEWED 01/08/20, 11/11/20, 10/13/21, 11/15/21, 05/11/22, 10/12/22, 07/12/23, 04/10/24	APPROVAL DATE April 10, 2024	EFFECTIVE DATE April 26, 2024	COMMITTEE APPROVAL DATES 01/08/20, 11/11/20, 10/13/21, 11/15/21, 05/11/22, 10/12/22, 07/12/23, 04/10/24	
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	

I. PURPOSE

To define and describe the accepted indications for Brukinsa (zanubrutinib) 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 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. B-Cell Lymphomas (Mantle Cell Lymphoma, Nodal/Extra-nodal/Splenic Marginal Zone Lymphoma)

1. The member has mantle cell lymphoma or nodal/extra-nodal/splenic marginal zone lymphoma **AND** Brukinsa (zanubrutinib) will be used as monotherapy in members with disease progression on at least one prior treatment, including an anti-CD20 agent (e.g., rituximab/rituximab biosimilar).

C. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

1. Brukinsa (zanubrutinib) may be used as monotherapy for initial or subsequent line therapy.

D. Waldenström's Macroglobulinemia (WM)

1. The member has a diagnosis of Waldenström's Macroglobulinemia (WM) and Brukinsa (zanubrutinib) will be used as monotherapy as initial therapy or therapy for relapsed disease.

E. Follicular Lymphoma

1. Brukinsa (zanubrutinib) may be used with obinutuzumab in members with relapsed or refractory follicular lymphoma who have failed on two or more lines of systemic therapy.

III. EXCLUSION CRITERIA

- A. Brukinsa (zanubrutinib) is being used after disease progression with the same regimen or prior disease progression on BTK inhibitor (e.g., ibrutinib, acalabrutinib).
- B. Dosing exceeds single dose limit of Brukinsa (zanubrutinib) 320 mg.
- C. Treatment exceeds the maximum limit of 120 (80mg) capsules/month.
- D. Investigational use of Brukinsa (zanubrutinib) 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. Tam CS, et al. Zanubrutinib versus bendamustine and rituximab in untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (SEQUOIA): a randomised, controlled, phase 3 trial. *Lancet Oncol.* 2022 Aug;23(8):1031-1043.
- B. Brown J, et al. SEQUOIA Clinical Trial ARM C. Efficacy and Safety of Zanubrutinib in Patients with Treatment-Naïve (TN) Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL) with del(17p): Follow-up Results from Arm C of the SEQUOIA (BGB-3111-304) Trial. *Blood.* 2020;136(suppl1):11-12.
- C. Hillmen P, et al. ALPINE Clinical Trial: zanubrutinib versus ibrutinib in relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma. *Future Oncol.* 2020 Apr;16(10):517-523. Brukinsa prescribing information. BeiGene USA, Inc. San Mateo, CA 2022.
- D. Zinzani P, et al. ROSEWOOD: A Phase II Randomized Study of Zanubrutinib Plus Obinutuzumab Versus Obinutuzumab Monotherapy in Patients With Relapsed or Refractory Follicular Lymphoma. *J Clin Oncol.* 2023; 41:5107-5117. DOI <https://doi.org/10.1200/JCO.23.00775>
- E. Clinical Pharmacology Elsevier Gold Standard 2023.
- F. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.
- G. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.
- H. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.
- I. 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.
- J. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>.