

## Brukinsa<sup>®</sup> (zanubrutinib) (Oral)

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### I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

### II. Dosing Limits

#### A. Quantity Limit (max daily dose) [NDC Unit]:

- Brukinsa 80 mg capsule: 4 capsules per day

#### B. Max Units (per dose and over time) [HCPCS Unit]:

- 320 mg per day

### III. Initial Approval Criteria <sup>1</sup>

Coverage is provided for the following conditions:

- Patient is at least 18 years of age; **AND**

#### Universal Criteria <sup>1</sup>

- Patient will avoid concomitant therapy with all of the following:
  - Coadministration with moderate or strong CYP3A inducers (e.g., rifampin, carbamazepine, St. John's Wort, phenobarbital, etc.); **AND**
  - Coadministration with moderate or strong CYP3A inhibitors (e.g., itraconazole, clarithromycin, diltiazem, etc.), or if therapy is unavoidable, the patient will be monitored closely for adverse reaction and/or dose modifications will be implemented; **AND**

#### B-Cell Lymphomas <sup>1,2,11</sup>

- Mantle Cell Lymphoma (MCL) † ⊕ <sup>1,2</sup>
  - Used as a single agent; **AND**
  - Patient has received at least one prior therapy
- Marginal Zone Lymphomas † ‡ <sup>1,2</sup>

- Used as a single agent as subsequent therapy after at least one prior anti-CD20 monoclonal antibody-based regimen (e.g., rituximab, obinutuzumab, ofatumumab, etc.); **AND**
- Patient has one of the following:
  - Gastric MALT lymphoma that is relapsed, refractory, or progressive
  - Nongastric (noncutaneous) MALT lymphoma that is relapsed, refractory, or progressive
  - Nodal marginal zone lymphoma that is relapsed, refractory, or progressive **Φ**
  - Splenic marginal zone lymphoma that is relapsed or refractory **Φ**

#### **Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma (WM/LPL) † ‡ **Φ** 1,2,5**

- Used as a single agent; **OR**
- Patient has symptomatic Bing-Neel syndrome; **AND**
  - Used as a single agent or in combination with rituximab if systemic control is needed

#### **Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia (CLL/SLL) ‡ 2,6,7**

- Used as a single agent; **AND**
- Patient does NOT have ibrutinib-refractory disease with BTK C481S mutations\*; **AND**
  - Used as first-, second- or third-line therapy for disease without del(17p)/TP53 mutation; **OR**
  - Used for disease with del(17p)/TP53 mutation

***\*NOTE:** Testing for BTK and PLCG2 mutations may be useful in patients with disease progression or no response while on BTK inhibitor therapy including if poor compliance is considered a possible cause. BTK and PSCG2 mutation status alone is not an indication to change treatment.*

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); **Φ** Orphan Drug

## **IV. Renewal Criteria** <sup>1</sup>

Coverage can be renewed based upon the following criteria:

- Patients continues to meet universal and other indication-specific relevant criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: hemorrhage, severe infections, myelosuppression (neutropenia, thrombocytopenia, anemia), atrial fibrillation/flutter, second primary malignancies, etc.; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

## V. Dosage/Administration <sup>1,6,11-13</sup>

Indication	Dose
MCL, MZL, WM/LPL	Administer 160 mg orally twice daily or 320 mg orally once daily, until disease progression or unacceptable toxicity. <i>* Refer to prescribing information for dose adjustments.</i>
CLL/SLL	Administer 160 mg orally twice daily until disease progression or unacceptable toxicity.

## VI. Billing Code/Availability Information

### HCPCS Code:

- J8999 - Prescription drug, oral, chemotherapeutic, Not Otherwise Specified
- C9399 – Unclassified drugs or biologicals (Hospital-Outpatient Prospective Payer System Use Only-HOPPS)

### NDC:

- Brukinsa 80 mg capsule: 72579-0011-xx

## VII. References

1. Brukinsa [package insert]. San Mateo, CA; BeiGene USA, Inc. September 2021. Accessed September 2022.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for zanubrutinib. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2022.
3. Tam CS, Trotman J, Opat S, et al. Phase 1 study of the selective BTK inhibitor zanubrutinib in B-cell malignancies and safety and efficacy evaluation in CLL. *Blood*. 2019 Sep 12;134(11):851-859. doi: 10.1182/blood.2019001160. Epub 2019 Jul 24.
4. Song Y, Zhou K, Zhou J, et al. Safety and Activity of the Investigational Bruton Tyrosine Kinase Inhibitor Zanubrutinib (BGB-3111) in Patients with Mantle Cell Lymphoma from a Phase 2 Trial. *Blood* 132(Suppl\_1):148-148 · Nov 2018. DOI: 10.1182/blood-2018-99-117956
5. Tam C, Opat S, D'Sa S, et al. A randomized phase 3 trial of zanubrutinib vs ibrutinib in symptomatic Waldenström macroglobulinemia: the ASPEN study. *Blood* (2020) 136 (18): 2038–2050. <https://doi.org/10.1182/blood.2020006844>
6. Tam C, Robak T, Ghia P, et al. Zanubrutinib monotherapy for patients with treatment naïve chronic lymphocytic leukemia and 17p deletion. *Haematologica*. 2020 Oct 13;106(9):2354-2363. doi: 10.3324/haematol.2020.259432.

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8. Song Y, Zhou K, Zhou D, et al. Treatment of Patients with Relapsed or Refractory Mantle-Cell Lymphoma with Zanubrutinib, a Selective Inhibitor of Bruton's Tyrosine Kinase. *Clin Cancer Res.* 2020 Aug 15;26(16):4216-4224. Epub 2020 May 27. doi: 10.1158/1078-0432.CCR-19-3703.
9. Opat S, Tedeschi A, Linton K, et al. Efficacy and Safety of Zanubrutinib in Patients with Relapsed/Refractory Marginal Zone Lymphoma: Initial Results of the MAGNOLIA (BGB-3111-214) Trial. *Blood* (2020) 136 (Supplement 1): 28–30. <https://doi.org/10.1182/blood-2020-134611>
10. Tam CS, Opat S, Simpson D, et al. Zanubrutinib for the treatment of relapsed or refractory mantle cell lymphoma. *Blood Adv.* 2021 Jun 22;5(12):2577-2585. doi: 10.1182/bloodadvances.2020004074.
11. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) B-Cell Lymphomas. Version 5.2022. National Comprehensive Cancer Network, 2022. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed September 2022.
12. Hillmen P, Eichhorst B, Brown J, et al. First interim analysis of the ALPINE study: a phase III randomized trial of zanubrutinib vs. ibrutinib in patients with relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma [abstract]. EHA 2021 LBA 1900.
13. Tam CS, Brown JR, Kahl BS, 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. doi: 10.1016/S1470-2045(22)00293-5.

## Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C83.00	Small cell B-cell lymphoma, unspecified site
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face, and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes

ICD-10	ICD-10 Description
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C83.10	Mantle cell lymphoma, unspecified site
C83.11	Mantle cell lymphoma, lymph nodes of head, face, and neck
C83.12	Mantle cell lymphoma, intrathoracic lymph nodes
C83.13	Mantle cell lymphoma, intra-abdominal lymph nodes
C83.14	Mantle cell lymphoma, lymph nodes of axilla and upper limb
C83.15	Mantle cell lymphoma, lymph nodes of inguinal region and lower limb
C83.16	Mantle cell lymphoma, intrapelvic lymph nodes
C83.17	Mantle cell lymphoma, spleen
C83.18	Mantle cell lymphoma, lymph nodes of multiple sites
C83.19	Mantle cell lymphoma, extranodal and solid organ sites
C83.80	Other non-follicular lymphoma, unspecified site
C83.81	Other non-follicular lymphoma, lymph nodes of head, face and neck
C83.82	Other non-follicular lymphoma, intrathoracic lymph nodes
C83.83	Other non-follicular lymphoma, intra-abdominal lymph nodes
C83.84	Other non-follicular lymphoma, lymph nodes of axilla and upper limb
C83.85	Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb
C83.86	Other non-follicular lymphoma, intrapelvic lymph nodes
C83.87	Other non-follicular lymphoma, spleen
C83.88	Other non-follicular lymphoma, lymph nodes of multiple sites
C83.89	Other non-follicular lymphoma, extranodal and solid organ sites
C85.87	Other specified types of non-Hodgkin lymphoma, spleen
C88.0	Waldenström macroglobulinemia
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma)
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse

## Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs), and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC