Brukinsa™ (zanubrutinib)
(Oral)

Document Number: IC-0511

Last Review Date: 10/01/2021
Date of Origin: 01/03/2020
Dates Reviewed: 01/2020, 11/2020, 10/2021

I. Length of Authorization

Coverage will be provided for six 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 [1]

Coverage is provided for the following conditions:

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

Universal Criteria [1]

- Used as single agent therapy; **AND**
- 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 [1,2]

- Mantle Cell Lymphoma (MCL) † Φ [1,2]
  - Patient has received at least one prior therapy

Proprietary & Confidential
© 2021 Magellan Health, Inc.

- Marginal Zone Lymphomas (Gastric or Nongastric MALT Lymphoma, Nodal MZL, or Splenic MZL) † ‡ [1,2]
  - Patient has relapsed or refractory disease; **AND**
  - Used as subsequent therapy after at least one prior anti-CD20 monoclonal antibody-based regimen (e.g., rituximab, obinutuzumab, ofatumumab, etc.)

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

Chronic Lymphocytic Leukemia/Small Lymphocytic Leukemia (CLL/SLL) ‡ [2,6,7]

- Patient does NOT have ibrutinib-refractory disease with BTK C481S mutations*; **AND**
  - Patient has a contraindication to treatment with other BTK-inhibitors (e.g., ibrutinib, acalabrutinib, etc.); **AND**
    - Used as first-line therapy for disease with del(17p)/TP53 mutation; **OR**
  - Patient has a contraindication or intolerance to treatment with other BTK-inhibitors (e.g., ibrutinib, acalabrutinib, etc.); **AND**
    - Used as subsequent therapy for disease with or without 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. 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 [1]

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

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

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

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 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for zanubrutinib. National Comprehensive Cancer Network, 2021. 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 2021.
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.
7. Xu W, Yang S, Zhou K, et al. Treatment of relapsed/refractory chronic lymphocytic leukemia/small lymphocytic lymphoma with the BTK inhibitor zanubrutinib: phase 2, single-arm, multicenter study. J Hematol Oncol. 2020; 13: 48. Epub 2020 May 11. doi: 10.1186/s13045-020-00884-4
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

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

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.

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
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

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management

ICD-10	ICD-10 Description
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

Proprietary Information. Restricted Access – Do not disseminate or copy without approval.
©2021, Magellan Rx Management