



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES  
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 2/13/2020  
LAST REVIEW DATE: 2/17/2022  
LAST CRITERIA REVISION DATE: 2/17/2022  
ARCHIVE DATE:

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## BRUKINSA™ (zanubrutinib) oral capsule

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Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "**Description**" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "**Criteria**" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy).

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the [request form](#) in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com). **Incomplete forms or forms without the chart notes will be returned.**

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### Criteria:

- **Criteria for initial therapy:** Brukinsa (zanubrutinib) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:

1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist
2. Individual is 18 years of age or older
3. A confirmed diagnosis of **ONE** of the following:
  - a. Mantle Cell Lymphoma (MCL) in those who have received at least one prior therapy
  - b. Waldenström's macroglobulinemia (WM)
  - c. Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen
  - d. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A
4. **ALL** of the following **baseline tests** have been completed before initiation of treatment with continued monitoring as clinically appropriate:
  - a. Negative pregnancy test in a woman of childbearing potential
  - b. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2
5. Individual does not have severe hepatic impairment
6. There are no significant interacting drugs

**Initial approval duration:** 6 months

- **Criteria for continuation of coverage (renewal request):** Brukinsa (zanubrutinib) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist
2. Individual's condition responded while on therapy
  - a. Response is defined as **ONE** of the following:
    - i. Documented evidence of efficacy, disease stability and/or improvement
    - ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use
3. Individual has been adherent with the medication



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4. Individual has not developed any significant adverse drug effects that may exclude continued use
  - a. Significant adverse effect such as:
    - i. Serious hemorrhagic events including intracranial, gastrointestinal, hematuria, or hemothorax
    - ii. Serious infection including bacterial, viral, or fungal and opportunistic infections
    - iii. Severe neutropenia, thrombocytopenia, leukopenia, or anemia

5. Individual does not have severe hepatic impairment

6. There are no significant interacting drugs

**Renewal duration:** 12 months

➤ Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-cancer Medications**
2. **Off-Label Use of Cancer Medications**

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### **Description:**

Brukinsa (zanubrutinib) is indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. Brukinsa (zanubrutinib) is also indicated for the treatment of adult patients with Waldenström's macroglobulinemia (WM). Brukinsa (zanubrutinib) is also indicated for the treatment of adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen. This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Brukinsa (zanubrutinib) is a highly selective Bruton tyrosine kinase (BTK) inhibitor (Tam 2019). Brukinsa (zanubrutinib) forms a covalent bond with a cysteine residue in the BTK active site to inhibit BTK activity. BTK is a signaling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. BTK signals activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion. Brukinsa (zanubrutinib) inhibits malignant B-cell proliferation and reduces tumor growth.



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### Definitions:

#### NCCN recommendation definitions:

Category 1:

Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:

Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:

Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:

Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

#### Common Terminology Criteria for Adverse Events (CTCAE) Version 4.0:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death related to AE
U.S. department of Health and Human Services, National Institutes of Health, and National Cancer Institute	

### Resources:

Brukinsa (zanubrutinib) product information, revised by BeiGene USA, Inc. 09-2021. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed December 02, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): B-Cell Lymphomas Version 5.2021 – Updated September 22, 2021. Available at <https://www.nccn.org>. Accessed December 02, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Waldenström’s Macroglobulinemia/Lymphoplasmacytic Lymphoma Version 1.2022 – Updated June 24, 2021. Available at <https://www.nccn.org>. Accessed December 02, 2021.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.