BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

BRUKINSA™ (zanubrutinib) oral capsule Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for BRUKINSA (zanubrutinib)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by an Oncologist or in consultation with an Oncologist

Indication
- Mantle Cell Lymphoma (mantle cell lymphoma) after at least one prior therapy
- Waldenström's Macroglobulinemia (Waldenström's macroglobulinemia)
- Relapsed or refractory Marginal Zone Lymphoma (marginal zone lymphoma) after at least one anti CD20 based regimen

ORIGINAL EFFECTIVE DATE: 02/13/2020 | ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 02/19/2026

- Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL)
- Relapsed or refractory Follicular Lymphoma (FL), in combination with Gazyva (obinutuzumab), after two or more lines of systemic therapy
- Other oncologic direct treatment uses listed in National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Bilirubin and transaminases
- Negative pregnancy test in a woman of childbearing potential
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 2

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- There is **NO** current use with strong CYP3A inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, others)

Additional Requirements
- Use of Brukinsa tablet with Brukinsa capsule will not be approved

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results (e.g., pregnancy test result, Eastern Cooperative Oncology Group Performance Status)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualifications
- Continues to be seen by an Oncologist or is in consultation with an Oncologist

Clinical Response
- Positive clinical response defined as no evidence of disease progression or unacceptable toxicity

PHARMACY COVERAGE GUIDELINE

BRUKINSA™ (zanubrutinib) oral capsule
Generic Equivalent (if available)

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No significant adverse drug effects such as:
  - Serious hemorrhagic events (intracranial, gastrointestinal, hematuria, hemothorax)
  - Serious infections (bacterial, viral, fungal, opportunistic)
  - Severe neutropenia, thrombocytopenia, leukopenia, or anemia
  - Serious cardiac arrhythmias
  - Hepatotoxicity including drug induced liver injury
- There is **NO** current use with strong CYP3A inducers (e.g., rifampin, rifabutin, phenobarbital, carbamazepine, others).

Additional Requirements
- Use of Brukinsa tablet with Brukinsa capsule will not be approved

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use from above criteria

Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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

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 also indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). Brukinsa (zanubrutinib) is also indicated for the treatment of adult patients with relapsed or refractory follicular lymphoma (FL), in combination with obinutuzumab, after two or more lines of systemic therapy.

Brukinsa (zanubrutinib) is a highly selective Bruton tyrosine kinase (BTK) inhibitor. 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.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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.

Eastern Co-operative Oncology Group (ECGO) Performance Status:

Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction
1	Restricted in physical strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work
2	Ambulatory and capable of all self-care but unable to carry out any work activities, up and about more than 50% of waking hours
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours
4	Completely disabled, cannot carry on any self-care, totally confined to bed or chair
5	Dead
Oken, MM, Creech, RH, Tormey, DC, et al.: Toxicity and Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

PHARMACY COVERAGE GUIDELINE

BRUKINSA™ (zanubrutinib) oral capsule
Generic Equivalent (if available)

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	

Bruton's kinase inhibitors:

Drug Name	FDA-Approved Uses
Calquence (acalabrutinib)	MCL, CLL/SLL
Imbruvica (ibrutinib)	MCL, CLL/SLL, WM, MZL, cGVHD
Jaypirca (pirtobrutinib)	MCL
Brukinsa (zanubrutinib)	MCL, WM, MZL
MCL = Mantle cell lymphoma CLL = Chronic lymphocytic leukemia SLL = Small lymphocytic lymphoma WM = Waldenström's macroglobulinemia MZL = Marginal zone lymphoma cGVHD = Chronic graft versus host disease	

Resources:

Brukinsa (zanubrutinib) product information, revised by BeOne Medicines USA, Inc. 06-2025. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed November 10, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): B-Cell Lymphomas Version 1.2026 – Updated December 22, 2025. Available at https://www.nccn.org. Accessed January 03, 2026.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma Version 1.2026 – Updated June 24, 2025. Available at https://www.nccn.org. Accessed January 03, 2026.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 2.2026 –Updated December 22, 2025. Available at https://www.nccn.org. Accessed January 03, 2026.

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.