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| **Section:** | Prescription Drugs | **Effective Date:** | April 1, 2024 |
| **Subsection:** | Antineoplastic Agents | **Original Policy Date:** | December 13, 2019 |
| **Subject:** | Brukinsa | **Page:** | 1 of 5 |

***Last Review Date:*** March 8, 2024

# Brukinsa

## Description

### Brukinsa (zanubrutinib)

**Background**
Brukinsa (zanubrutinib) is a small-molecule inhibitor of Bruton's tyrosine kinase (BTK). Brukinsa forms a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK activity. BTK is a signaling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. In B-cells, BTK signaling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion. Brukinsa inhibits malignant B-cell proliferation and reduced tumor growth (1).

**Regulatory Status**
FDA-approved indications: Brukinsa is a kinase inhibitor indicated for the treatment of adult patients with: (1)

- Mantle cell lymphoma (MCL) who have received at least one prior therapy.
- Waldenström's macroglobulinemia (WM).
- Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen.
- Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)

Fatal and serious hemorrhagic events have occurred in patients with hematological malignancies treated with Brukinsa monotherapy. Bleeding events have occurred in patients with and without concomitant antiplatelet of anticoagulation therapy. Co-administration of Brukinsa with antiplatelet or anticoagulant medication may further increase the risk of hemorrhage. Patients should be monitored for signs and symptoms of bleeding (1).

Significant adverse reactions may occur with Brukinsa therapy including fatal and serious infections, cytopenia, cardiac arrhythmias, and second primary malignancies including non-skin carcinoma. Patients should have the following monitored while on Brukinsa therapy: fever, infections, complete blood counts, and signs and symptoms for atrial fibrillation and atrial flutter (1).

Advise women to avoid becoming pregnant while taking Brukinsa and for at least 1 week after the last dose. Advise men to avoid fathering a child during treatment and for at least 1 week after the last dose. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus (1).

The safety and effectiveness of Brukinsa in pediatric patients less than 18 years of age have not been established (1).

**Related policies**
Calquence, Imbruvica, Jaypirca

## Policy

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Brukinsa may be considered **medically necessary** if the conditions indicated below are met.

Brukinsa may be considered **investigational** for all other indications.

## Prior-Approval Requirements

**Age** 18 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:

1. Mantle cell lymphoma (MCL)
    a. Patient has received at least one prior therapy
2. Waldenström's macroglobulinemia (WM)
3. Relapsed or refractory marginal zone lymphoma (MZL)

a. Patient has received at least one anti-CD20-based regimen

4. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)

**AND ALL** of the following:

a. Prescriber agrees to monitor for bleeding and malignancies
b. Prescriber agrees to monitor CBC for cytopenias
c. Prescriber agrees to monitor for cardiac arrhythmias
d. Females of reproductive potential **only**: patient will be advised not to become pregnant during treatment with Brukinsa and for at least 1 week after the last dose
e. Males with female partners of reproductive potential **only**: patient will be advised not to father a child during treatment with Brukinsa and for at least 1 week after the last dose

## Prior – Approval *Renewal* Requirements

**Age** 18 years of age or older

**Diagnoses**

Patient must have **ONE** of the following:

1. Mantle cell lymphoma (MCL)
2. Waldenström's macroglobulinemia (WM)
3. Relapsed or refractory marginal zone lymphoma (MZL)
4. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL)

**AND ALL** of the following:

a. **NO** disease progression or unacceptable toxicity
b. Prescriber agrees to monitor for bleeding and malignancies
c. Prescriber agrees to monitor CBC for cytopenias
d. Prescriber agrees to monitor for cardiac arrhythmias
e. Females of reproductive potential **only**: patient will be advised not to become pregnant during treatment with Brukinsa and for at least 1 week after the last dose
f. Males with female partners of reproductive potential **only**: patient will be advised not to father a child during treatment with Brukinsa and for at least 1 week after the last dose

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

**Quantity** 360 capsules per 90 days

**Duration** 12 months

### Prior – Approval *Renewal* Limits

Same as above

## Rationale

**Summary**

Brukinsa (zanubrutinib) is a small-molecule inhibitor of Bruton's tyrosine kinase (BTK). Brukinsa forms a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK activity. BTK is a signaling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. In B-cells, BTK signaling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion. Brukinsa inhibits malignant B-cell proliferation and reduced tumor growth. The safety and effectiveness of Brukinsa in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Brukinsa while maintaining optimal therapeutic outcomes.

**References**

1. Brukinsa [package insert]. San Mateo, CA: BeiGene USA, Inc.; December 2023.
2. NCCN Drugs & Biologics Compendium® Zanubrutinib 2024. National Comprehensive Cancer Network, Inc. Accessed on January 22, 2024.

## Policy History

| Date | Action |
|---|---|
| December 2019 | Addition to PA |

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| March 2020 | Annual review |
| March 2021 | Annual editorial review |
| September 2021 | Addition of indication: Waldenström's macroglobulinemia and relapsed or refractory marginal zone lymphoma |
| December 2021 | Annual review and reference update |
| March 2022 | Annual editorial review and reference update. Per FEP, added NCCN recommended use in CLL/SLL |
| December 2022 | Annual review and reference update |
| March 2023 | Annual editorial review and reference update. Added CLL/SLL as an FDA-approved indication rather than an off-label use |
| June 2023 | Annual review and reference update |
| March 2024 | Annual review and reference update |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.**