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Section:	Prescription Drugs	**Effective Date:**	October 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	December 13, 2019
Subject:	Brukinsa	**Page:**	1 of 5

Last Review Date: September 19, 2025

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).
- Relapsed or refractory follicular lymphoma (FL), in combination with obinutuzumab, after two or more lines of systemic therapy.

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 or 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)
5. Relapsed or refractory follicular lymphoma (FL)
    a. Patient has received two or more lines of systemic therapy
    b. Used in combination with Gazyva (obinutuzumab)

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)
5. Relapsed or refractory follicular lymphoma (FL)
    a. Used in combination with Gazyva (obinutuzumab)

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 320 mg per day

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.; June 2025.

2. NCCN Drugs & Biologics Compendium® Zanubrutinib 2025. National Comprehensive Cancer Network, Inc. Accessed on August 20, 2025.

Policy History

Date	Action
December 2019	Addition to PA
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
April 2024	Per PI update, added indication of FL in combination with obinutuzumab
June 2024	Annual review and reference update
March 2025	Annual review and reference update
July 2025	Per PI update, changed quantity limit to 320 mg per day
September 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 19, 2025 and is effective on October 1, 2025.