UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2024 P 3173-3
Program	Step Therapy
Medication	Brukinsa® (zanubrutinib)
P&T Approval Date	7/2023, 7/2024, 10/2024
Effective Date	1/1/2025

1. Background:

Step therapy programs are utilized to encourage use of lower cost alternatives for certain therapeutic classes. This program requires a member to try Calquence® (acalabrutinib) or Imbruvica® (ibrutinib) before providing coverage for Brukinsa® (zanubrutinib).

Brukinsa (zanubrutinib) is a kinase inhibitor indicated for the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy, relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen, and relapsed or refractory follicular lymphoma (FL), in combination with obinutuzumab, after two or more lines of systemic therapy. These indications are approved under accelerated approval based on overall response rate. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial. Brukinsa is also indicated for the treatment of Waldenström's macroglobulinemia (WM) and chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). The National Comprehensive Cancer Network (NCCN) recommends Brukinsa for relapsed/refractory hairy cell leukemia and as second-line and subsequent therapy for extranodal marginal zone lymphoma (EMZL) of the stomach, extranodal marginal zone lymphoma of nongastric sites (noncutaneous), nodal marginal zone, and splenic marginal zone lymphomas.

Calquence (acalabrutinib) is a kinase inhibitor indicated for the treatment of adult patients with 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 confirmatory trials. It is also approved for the treatment of adult patients with CLL or SLL. NCCN recommends the use of Calquence for the treatment of Waldenström macroglobulinemia/lymphoplasmacytic lymphoma, extranodal marginal zone lymphoma of the stomach, nodal marginal zone lymphoma, and splenic marginal zone lymphoma.

Imbruvica (ibrutinib) is a kinase inhibitor indicated for the treatment of patients with CLL/SLL, CLL/SLL with 17p deletion, WM, and adult and pediatric patients aged 1 year and older with chronic graft versus host disease after failure of one or more lines of systemic therapy. NCCN also recommends the use of Imbruvica for hairy cell leukemia, primary central nervous system lymphoma, extranodal marginal zone lymphoma of the sstomach, extranodal marginal zone lymphoma of nongastric sites (noncutaneous), nodal marginal zone lymphoma, splenic marginal zone lymphoma, MCL, diffuse large B-cell lymphoma, high-grade b-cell lymphoma, HIV-related B-cell lymphoma, and post-transplant lymphoproliferative disorders.

Members currently on Brukinsa therapy as documented in claims history will be allowed to continue on their current therapy. Members new to therapy will be required to meet the coverage criteria below.

Coverage Information:

Members will be required to meet the criteria below for coverage. For members under the age of 19 years, the prescription will automatically process without a coverage review.

Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances. Some states also mandate usage of other Compendium references. Where such mandates apply, they supersede language in the benefit document or in the notification criteria.

2. Coverage Criteria [a,b]:

A. Patients less than 19 years of age

1. **Brukinsa** will be approved based on the following criterion:

   a. Patient is less than 19 years of age

   Authorization will be issued for 12 months.

B. Mantle Cell Lymphoma (MCL)

1. **Brukinsa** will be approved based on **both** of the following:

   a. Diagnosis of mantle cell lymphoma

   -AND-

   b. **One** of the following:

      (1) Patient has a contraindication or history of intolerance to **one** of the following:

         (a) Calquence (acalabrutinib)

         (b) Imbruvica (ibrutinib)

      -OR-

      (2) Provider attests patient is not an appropriate candidate based on patient's clinical status or comorbidities for **both** of the following:

         (a) Calquence (acalabrutinib)

         (b) Imbruvica (ibrutinib)

      -OR-

      (3) **Both** of the following:

(a) As continuation of therapy

-AND-

(b) Patient has **not** received a manufacturer supplied sample at no cost from a prescriber's office, or any form of assistance from the BeiGene's myBeiGene sponsored patient support program (e.g., sample card which can be redeemed at a pharmacy for a free supply of medication) or a 30-day free trial from a pharmacy as a means to establish as a current user of Brukinsa

*Patients requesting initial authorization who were established on therapy via the receipt of a manufacturer supplied sample at no cost in the prescriber's office or any form of assistance from the BeiGene's myBeiGene sponsored patient support program **shall be required** to meet initial authorization criteria as if patient were new to therapy.

Authorization will be issued for 12 months.

C. Marginal Zone Lymphoma (MZL)

1. **Brukinsa** will be approved based on **both** of the following:

a. Diagnosis of marginal zone lymphoma

-AND-

b. **One** of the following:

(1) Patient has a contraindication or history of intolerance to **one** of the following:

(a) Calquence (acalabrutinib)

(b) Imbruvica (ibrutinib)

-OR-

(2) Provider attests patient is not an appropriate candidate based on patient's clinical status or comorbidities for **both** of the following:

(a) Calquence (acalabrutinib)

(b) Imbruvica (ibrutinib)

-OR-

(3) **Both** of the following:

(a) As continuation of therapy

-AND-

(b) Patient has **not** received a manufacturer supplied sample at no cost from a prescriber's office, or any form of assistance from the BeiGene's myBeiGene sponsored patient support program (e.g., sample card which can be redeemed at a pharmacy for a free supply of medication) or a 30-day free trial from a pharmacy as a means to establish as a current user of Brukinsa

*Patients requesting initial authorization who were established on therapy via the receipt of a manufacturer supplied sample at no cost in the prescriber's office or any form of assistance from the BeiGene's myBeiGene sponsored patient support program **shall be required** to meet initial authorization criteria as if patient were new to therapy.

Authorization will be issued for 12 months.

D. Waldenström Macroglobulinemia

1. **Brukinsa** will be approved based on **both** of the following:

a. Diagnosis of Waldenström macroglobulinemia

-AND-

b. **One** of the following:

(1) Patient has a contraindication or history of intolerance to **one** of the following:

(a) Calquence (acalabrutinib)

(b) Imbruvica (ibrutinib)

-OR-

(2) Provider attests patient is not an appropriate candidate based on patient's clinical status or comorbidities for **both** of the following:

(a) Calquence (acalabrutinib)

(b) Imbruvica (ibrutinib)

-OR-

(3) **Both** of the following:

(a) As continuation of therapy

-AND-

(b) Patient has **not** received a manufacturer supplied sample at no cost from a prescriber's office, or any form of assistance from the BeiGene's

myBeiGene sponsored patient support program (e.g., sample card which can be redeemed at a pharmacy for a free supply of medication) or a 30-day free trial from a pharmacy as a means to establish as a current user of Brukinsa

*Patients requesting initial authorization who were established on therapy via the receipt of a manufacturer supplied sample at no cost in the prescriber's office or any form of assistance from the BeiGene's myBeiGene sponsored patient support program **shall be required** to meet initial authorization criteria as if patient were new to therapy.

Authorization will be issued for 12 months.

E. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL)

1. **Brukinsa** will be approved based on **both** of the following:

   a. Diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma

   -AND-

   b. **One** of the following:

      (1) Patient has a contraindication or history of intolerance to **one** of the following:

         (a) Calquence (acalabrutinib)

         (b) Imbruvica (ibrutinib)

      -OR-

      (2) Provider attests patient is not an appropriate candidate based on patient's clinical status or comorbidities for **both** of the following:

         (a) Calquence (acalabrutinib)

         (b) Imbruvica (ibrutinib)

      -OR-

      (3) **Both** of the following:

         (a) As continuation of therapy

         -AND-

         (b) Patient has **not** received a manufacturer supplied sample at no cost from a prescriber's office, or any form of assistance from the BeiGene's myBeiGene sponsored patient support program (e.g., sample card which can be redeemed at a pharmacy for a free supply of medication) or a 30-day free trial from a pharmacy as a means to establish as a current user of Brukinsa

*Patients requesting initial authorization who were established on therapy via the receipt of a manufacturer supplied sample at no cost in the prescriber's office or any form of assistance from the BeiGene's myBeiGene sponsored patient support program **shall be required** to meet initial authorization criteria as if patient were new to therapy.

Authorization will be issued for 12 months.

F. Other Indications

1. **Brukinsa** will be approved.

   Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.
[b] Coverage of oncology medications may be approved based on state mandates.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits and/or Notification may be in place.
- Coverage of oncology medications may be approved based on state mandates.

4. References:

1. Brukinsa [package insert]. San Mateo, CA: BeiGene, Ltd.; March 2024.
2. Calquence [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP. August 2022.
3. Imbruvica [package insert]. South San Francisco, CA: Pharmacyclics, LLC; May 2024.
4. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Available at NCCN Drugs and Biologics Compendium®. Accessed May 31, 2024.

Program	Step Therapy - Brukinsa (zanubrutinib)
Change Control	
7/2023	New program
7/2024	Annual review with no changes to step criteria. Updated background and references.
10/2024	Updated criteria from either to both to clarify verbiage with no change in clinical intent.