PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Brukinsa Prior Authorization Policy
- Brukinsa® (zanubrutinib capsules – BeiGene)

REVIEW DATE: 04/19/2023

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Brukinsa, a Bruton's tyrosine kinase inhibitor (BTK), is indicated for the treatment of the following conditions: [1]

- **Chronic lymphocytic leukemia or small lymphocytic lymphoma,** in adults.
- **Mantle cell lymphoma,** in adults who have received at least one prior therapy.
- **Marginal zone lymphoma** relapsed or refractory, in adults who have received at least one anti-CD20-based regimen.
- **Waldenström's Macroglobulinemia,** in adults.

Guidelines

Brukinsa is discussed in guidelines from the National Comprehensive Cancer Network (NCCN):[4]

- **B-Cell Lymphomas**: NCCN guidelines (version 2.2023 – February 8, 2023) address marginal zone lymphoma and mantle cell lymphoma.[2] The guidelines recommend Brukinsa as a "Preferred Regimen" among several as second-line and subsequent therapy for marginal zone lymphoma for patients who have relapsed/refractory disease after at least one prior anti-CD20 monoclonal antibody (mAB)-based regimen (category 2A). For mantle cell lymphoma, Brukinsa is a "Preferred Regimen" for second-line or subsequent therapy

(category 2A). There is a footnote that states that Brukinsa or Calquence has not been shown to be effective for Imbruvica-refractory mantle cell lymphoma with *BTK* C481S mutations. Patients with Imbruvica intolerance have been successfully treated with Brukinsa or Calquence without recurrence of symptoms.

- **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma:** NCCN guidelines (version 2.2023 – January 25, 2023) recommend single-agent Brukinsa as first-line "Preferred Regimen" for patients without 17p deletion/TP53 mutation (category 1) and with 17p deletion/TP53 mutation (category 2A). Brukinsa is also recommended as second-line and subsequent therapy "Preferred Regimen" for patients with or without 17p deletion/TP53 mutation (category 1).[3] In the second-line and subsequent therapy setting, there is a footnote, which states that Brukinsa or Calquence have not been shown to be effective for Imbruvica-refractory chronic lymphocytic leukemia with BTK C481S mutations. Patients with Imbruvica intolerance have been successfully treated with Brukinsa or Calquence without recurrence of symptoms.
- **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma**: NCCN guidelines (version 1.2023 – July 6, 2022) recommend single-agent Brukinsa as a primary "Preferred Therapy" (category 1).[5] The guidelines also recommend Brukinsa as a "Preferred Therapy" option for previously treated disease (category 1). Brukinsa is also recommended for symptomatic management of Bing Neel Syndrome as a "Preferred Regimen" (category 2A).

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Brukinsa. All approvals are provided for the duration noted below.

- **Brukinsa® (zanubrutinib capsules (BeiGene)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Chronic Lymphocytic Leukemia.** Approve for 1 year if the patient is ≥ 18 years of age.

2. **Mantle Cell Lymphoma.** Approve for 1 year if the patient meets the following criteria (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets one of the following criteria (i or ii):
      i. Patient has tried at least one systemic regimen; OR
      Note: Examples of a systemic regimen contain one or more of the following products: rituximab, dexamethasone, cytarabine, carboplatin, cisplastin,

oxaliplatin, cyclophosphamide, doxorubicin, vincristine, prednisone, methotrexate, bendamustine, bortezomib, lenalidomide

ii. According to the prescriber, patient is not a candidate for a systemic regimen (i.e., an elderly patient who is frail).

3. **Marginal Zone Lymphoma**. Approve for 1 year if the patient meets the following criteria (A and B):
   Note: Marginal zone lymphoma includes gastric MALT lymphoma, non-gastric MALT lymphoma, nodal marginal zone lymphoma, and splenic marginal zone lymphoma.
   A) Patient is ≥ 18 years of age; AND
   B) Patient has tried at least one systemic regimen.
   Note: Examples of a systemic regimen contain one or more of the following products: bendamustine, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone, lenalidomide, Gazyva (obinutuzumab intravenous infusion) or Imbruvica (ibrutinib tablets and capsules).

4. **Small Lymphocytic Lymphoma.** Approve for 1 year if the patient is ≥ 18 years of age.

5. **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma.** Approve for 1 year if the patient is ≥ 18 years of age.

CONDITIONS NOT COVERED

- **Brukinsa® (zanubrutinib capsules (BeiGene)**

is(are) considered experimental, investigational or unproven for ANY other use(s).

REFERENCES

1. Brukinsa™ capsules [prescribing information]. San Mateo, CA: BeiGene; January 2023.
2. The NCCN B-Cell Lymphomas Guidelines in Oncology (version 2.2023 – February 8, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on April 12, 2023.
3. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 2.2023 – January 25, 2023). © 2023 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on April 12, 2023.
4. The NCCN Drugs and Biologics Compendium. © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed April 12, 2023. Search term: zanubrutinib.
5. The NCCN Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2023 – July 6, 2022). © 2022 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on April 12, 2023.

HISTORY

Type of Revision	Summary of Changes	Review Date

Early Annual Revision	**Marginal Zone Lymphoma:** The requirement that according to the prescriber, the patient has intolerance or contraindication to Imbruvica (ibrutinib capsules or tablets) was removed. **Chronic Lymphocytic Leukemia:** The requirement that the patient has tried at least one systemic regimen was removed. **Small Lymphocytic Lymphoma:** The requirement that the patient has tried at least one systemic regimen was removed.	05/04/2022
Selected Revision	**Mantle Cell Lymphoma:** The duration of approval was changed from 3 years to 1 year. **Marginal Zone Lymphoma:** The duration of approval was changed from 3 years to 1 year. **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma:** The duration of approval was changed from 3 years to 1 year. **Chronic Lymphocytic Leukemia:** The duration of approval was changed from 3 years to 1 year. **Small Lymphocytic Lymphoma:** The duration of approval was changed from 3 years to 1 year.	06/22/2022
Update	**01/20/2023: Chronic Lymphocytic Leukemia:** Condition of approval was moved from Other Uses with Supportive Evidence and into the FDA labeled indications section due to new FDA approved indication. **Small Lymphocytic Lymphoma:** Condition of approval was moved from Other Uses with Supportive Evidence and into the FDA labeled indications section due to new FDA approved indication.	--
Early Annual Revision	**Mantle Cell Lymphoma:** An alternative option of approval was added to the requirement for a trial of one systemic regimen that according to the prescriber, the patient is not a candidate for a systemic regimen (i.e., an elderly person who is frail).	04/19/2023