

PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Brukinsa Prior Authorization Policy

- Brukinsa® (zanubrutinib capsules – BeiGene)

REVIEW DATE: 03/13/2024; selected revision 06/12/2024

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.
- **Follicular lymphoma**, relapsed or refractory, in combination with Gazyva® (obinutuzumab intravenous infusion), after two or more lines of systemic therapy 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 1.2024 – January 18, 2024) address classic follicular lymphoma, marginal zone lymphoma, and mantle cell lymphoma.² The guidelines recommend Brukinsa + Gazyva as third-line and subsequent therapy as “Other Recommended Regimens” for classic follicular lymphoma (category 2A). 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 (acalabrutinib tablets) 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. Rituximab + covalent BTK inhibitors (Calquence, Imbruvica [ibrutinib tablets, capsules, or oral solution], or Brukinsa) can be used as pre-treatment in order to limit the number of cycles of induction therapy with R-HyperCVAD regimen (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone) [category 2A]. Brukinsa in combination with Venclexta (venetoclax tablets) and Gazyva® (obinutuzumab intravenous infusion) is also recommended as induction therapy for mantle cell lymphoma with a classical or indolent *TP53* mutation (category 2A) in absence of a clinical trial.⁵
 - **Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma:** NCCN guidelines (version 2.2024 – March 11, 2024) 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.
-

- **Hairy Cell Leukemia:** NCCN guidelines (version 1.2024 – November 3, 2023) recommend single-agent Brukinsa for patients with progressive disease after relapsed/refractory therapy as “Other Recommended Regimens” (category 2A).⁵
- **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma:** NCCN guidelines (version 2.2024 – December 5, 2023) recommend single-agent Brukinsa as a primary “Preferred Regimen” (category 1).⁶ The guidelines also recommend Brukinsa as a “Preferred Regimen” 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Brukinsa is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Chronic Lymphocytic Leukemia.** Approve for 1 year if the patient is ≥ 18 years of age.
2. **Follicular Lymphoma.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
 - A) Patient is ≥ 18 years of age; AND
 - B) Patient has tried at least two other systemic regimens AND
Note: Examples of systemic regimens contain one or more of the following products: bendamustine, Gazyva (obinutuzumab intravenous infusion), rituximab, cyclophosphamide, vincristine, prednisone, lenalidomide, chlorambucil, or Tazverik (tazemetostat tablets).
 - C) This medication will be used in combination with Gazyva (obinutuzumab intravenous infusion).
3. **Mantle Cell Lymphoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
 - A) Patient is ≥ 18 years of age; AND
 - B) Patient meets ONE of the following (i, ii, iii, or iv):
 - 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, cisplatin, 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 patients who is frail); OR
 - iii. Patient meets BOTH of the following (a and b):
 - a) This medication is being used in combination with rituximab; AND
 - b) This medication is being used as pre-treatment in order to limit the number of cycles of induction therapy with RHyperCVAD regimen (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone).
 - iv. Patient meets BOTH of the following (a and b):
 - a) Patient has a TP53 mutation; AND
 - b) The medication is used as induction therapy in combination with Venclexta (venetoclax tablets) and Gazyva (obinutuzumab intravenous infusion).

4. **Marginal Zone Lymphoma.** Approve for 1 year if the patient meets BOTH of the following (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, capsules, or oral solution).

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

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

Other Uses with Supportive Evidence

7. **Hairy Cell Leukemia.** Approve for 1 year if the patient meets ALL of the following (A, B and C):

A) Patient is ≥ 18 years of age; AND

B) Patient has received at least one systemic therapy for relapsed or refractory disease; AND

Note: Examples of therapy include: clinical trial, Tafinlar (dabrafenib capsules or oral tablets for suspension) + Mekinist (trametinib tablets), Zelboraf (vemurafenib tablets), rituximab, Pegasys (peginterferon alfa-2a subcutaneous injection), cladribine, Nipent (pentostatin intravenous infusion).

C) Patient has progressive disease.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Brukinsa is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Brukinsa[®] capsules [prescribing information]. San Mateo, CA: BeiGene; March 2024..
2. The NCCN B-Cell Lymphomas Guidelines in Oncology (version 1.2024 – January 18, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on March 12, 2024.
3. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 2.2024 – March 11, 2024). © 2024 National Comprehensive Cancer Network. Available at <http://www.nccn.org>. Accessed on March 12, 2024.
4. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed March 12, 2024. Search term: zanubrutinib.
5. The NCCN Hairy Cell Leukemia Clinical Practice Guidelines in Oncology (version 1.2024 – November 3, 2023). © 2023 National Comprehensive Cancer Network. Available at <http://www.nccn.org>. Accessed on March 12, 2024.
6. The NCCN Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 2.2024 – December 5, 2023). © 2023 National Comprehensive Cancer Network. Available at <http://www.nccn.org>. Accessed on March 12, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
------------------	--------------------	-------------

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
Early Annual Revision	Follicular Lymphoma: Condition of approval and criteria were added to FDA-approved indication section due to new FDA indication for relapsed or refractory follicular lymphoma, in combination with Gazyva® (obinutuzumab intravenous infusion), after two or more lines of systemic therapy in adults. Mantle Cell Lymphoma: Criteria which states that this medication is being used in combination with rituximab and being used as pre-treatment in order to limit the number of cycles of induction therapy with RHyperCVAD regimen (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone) was added an option for approval. Hairy Cell Leukemia: Condition of approval and criteria were added to Other Uses with Supportive Evidence.	03/13/2024
Selected Revision	Mantle Cell Lymphoma: The following criteria were added as an option for approval, “Patient has a <i>TP53</i> mutation and the medication is used as induction therapy in combination with Venclexta (venetoclax tablets) and Gazyva (obinutuzumab intravenous infusion).”	06/12/2024