Clinical Policy: Zanubrutinib (Brukinsa)

Reference Number: CP.PHAR.467
Effective Date: 03.01.20
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Zanubrutinib (Brukinsa™) is a Bruton tyrosine kinase (BTK) inhibitor.

FDA Approved Indication(s)

Brukinsa is indicated for the treatment of adult patients with:

- 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*

**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.*

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Brukinsa is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Mantle Cell Lymphoma (must meet all)**:**

1. Diagnosis of MCL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For brand Brukinsa requests, member must use generic zanubrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Member has received ≥ 1 prior therapy (*see Appendix B)*;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 320 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Waldenström's Macroglobulinemia (must meet all)**:**
1. Diagnosis of WM;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For brand Brukinsa requests, member must use generic zanubrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Brukinsa is not prescribed concurrently with Imbruvica®;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 320 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. Marginal Zone Lymphoma (*B-cell lymphoma subtype*) (must meet all)**:**
1. Diagnosis of one of the following MZL subtypes (a, b, c, or d):
   a. Gastric MALT lymphoma;
   b. Nongastric MALT lymphoma (noncutaneous);
   c. Nodal MZL;
   d. Splenic MZL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For brand Brukinsa requests, member must use generic zanubrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Member has received ≥ 1 line of systemic therapy* *(see Appendix B*);
   **Prior authorization may be required*
6. Brukinsa is not prescribed concurrently with Imbruvica;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 320 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (off-label) (must meet all):
1. Diagnosis of CLL/SLL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Member has intolerance or contraindication to other BTK inhibitors (e.g., ibrutinib, acalabrutinib);
5. For brand Brukinsa requests, member must use generic zanubrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 320 mg (4 capsules) per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

E. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Brukinsa for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand Brukinsa requests, member must use generic zanubrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 320 mg (4 capsules) per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BTK: Bruton tyrosine kinase
CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
MCL: mantle cell lymphoma
MZL: marginal zone lymphoma
NCCN: National Comprehensive Cancer Network
SLL: small lymphocytic lymphoma
WM: Waldenström's macroglobulinemia

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
MCL		
CALGB (rituximab + methotrexate + cyclophosphophamide, doxorubicin, vincristine, prednisone; etoposide, cytarabine, rituximab; carmustine, etoposide, cyclophosphamide/autologous stem cell rescue; rituximab)	Varies	Varies
HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone/methotrexate/ cytarabine) + rituximab	Varies	Varies
NORDIC (rituximab + cyclophosphamide, vincristine, doxorubicin, prednisone/rituximab + cytarabine)	Varies	Varies
RCHOP/RDHAP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)/(rituximab, dexamethasone, cisplatin, cytarabine)	Varies	Varies
RDHAP (rituximab, dexamethasone, cisplatin, cytarabine)	Varies	Varies
RCHOP/RICE (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)/(rituximab, ifosfamide, carboplatin, etoposide)	Varies	Varies
Bendeka® (bendamustine) + Rituxan® (rituximab)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)	Varies	Varies
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituxan® (rituximab)	Varies	Varies
Revlimid® (lenalidomide) + Rituxan® (rituximab)	Varies	Varies
CLL/SLL		
Calquence® (acalabrutinib)	100 mg PO BID	400 mg/day
Imbruvica® (ibrutinib)	420 mg PO QD	420 mg/day
WM		
bendamustine/rituximab, Imbruvica® +/- rituximab	Varies	Varies
MZL		
Bendeka® (bendamustine) + Rituxan® (rituximab)	Varies	Varies
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituxan® (rituximab)	Varies	Varies
CVP (cyclophosphamide, vincristine, prednisone) + Rituxan® (rituximab)	Varies	Varies
Rituxan® (rituximab)	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MCL, WM, MZL	160 mg PO BID or 320 mg PO QD	320 mg/day

VI. Product Availability

Capsule: 80 mg

VII. References

1. Brukinsa Prescribing Information. San Mateo, CA; BeiGene USA, Inc.; September 2021. Available at www.brukinsa.com. Accessed October 14, 2021.
2. Zanubrutinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed October 14, 2021.
3. National Comprehensive Cancer Network Guidelines. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma. Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed October 14, 2021.
4. National Comprehensive Cancer Network Guidelines. B-cell lymphomas Version 5.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed October 14, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.07.20	02.20
1Q 2021 annual review: oral oncology generic redirection language added; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.09.20	02.21
Added off-label indication for CLL/SLL per NCCN guidelines.	05.07.21	
1Q 2022 annual review: RT4: criteria added for new FDA approved indications: WM and MZL; modified "Medical justification…" to "Member must use…"; references reviewed and updated.	10.14.21	02.22
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible

for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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