Clinical Policy: Zanubrutinib (Brukinsa)

Reference Number: ERX.SPA.373
Effective Date: 03.01.20
Last Review Date: 02.21
Line of Business: Commercial, 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.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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. Member has received ≥ 1 prior therapy (*see Appendix B)*;
5. 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:
Commercial – Length of Benefit
Medicaid – 6 months

B. 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 request, medical justification supports inability to use generic zanubrutinib, if available, (e.g., contraindications to excipients);
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:
Commercial – Length of Benefit
Medicaid – 6 months

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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. 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:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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
NCCN: National Comprehensive Cancer Network
SLL: small lymphocytic lymphoma

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Mantle Cell Lymphoma		
CALGB (rituximab + methotrexate + cyclophosphosphamide, doxorubicin, vincristine, prednisone; etoposide, cytarabine, rituximab; carmustine, etoposide, cyclophosphamide/autologous stem cell rescue; rituximab)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
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

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	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.; November 2019. Available at www.brukinsa.com. Accessed November 9, 2020.
2. Zanubrutinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed May 7, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.07.20	02.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	11.09.20	02.21
Added off-label indication for CLL/SLL per NCCN guidelines.	05.07.21	

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.