Clinical Policy Title:	zanubrutinib
Policy Number:	RxA.620
Drug(s) Applied:	Brukinsa®
Original Policy Date:	05/21/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

Background

Brukinsa® is a kinase inhibitor 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 a confirmatory trial.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
zanubrutinib (Brukinsa®)	Mantle cell lymphoma, following at least 1 prior therapy	160 mg orally twice daily or 320 mg once daily	320mg

Dosage Forms

- Oral capsule: 80 mg

Clinical Policy

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

I. Initial Approval Criteria

A. B-Cell Lymphoma (must meet all):

1. Member has one of the following type of B-cell lymphoma diagnosis:
   a. Mantle cell lymphoma;
   b. Gastric MALT Lymphoma
   c. Nodal marginal zone lymphoma
   d. Splenic marginal zone lymphoma
   e. Non-gastric MALT lymphoma (non-cutaneous)
2. Member is 18 years of age or older;
3. Member has received at least one prior first line therapy (as listed in Appendix B or per NCCN guidelines);
4. Member is intolerant to or have contraindications to ibrutinib;
5. Prescribed by or in consultation with an oncologist or hematologist;

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: 6 months
Medicaid: 6 months

B. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (must meet all):

1. Diagnosis of CLL/SLL;
2. Member is 18 years or older;
3. Prescribed as monotherapy for one of the following (a or b):
   a. CLL/SLL with del(17p)/TP53 mutation in members with contraindication to other bruton tyrosine kinase (BTK) inhibitors who have indications for treatment;
   b. CLL/SLL with or without del(17p)/TP53 mutation in patients with intolerance or contraindication to other BTK inhibitors who have indications for retreatment;
4. Prescribed by or in consultation with an oncologist or hematologist;
5. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration:
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. The member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. The prescriber has reassessed efficacy and established goals of therapy;
3. The member is responding positively to therapy;
4. Requested dose is either FDA approved or supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration:
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
MCL: Mantle cell lymphoma
BTK: Bruton's tyrosine kinase
CLL: Chronic Lymphocytic Leukemia
SLL: Small Lymphocytic Leukemia
FDA: Food and Drug Administration

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
CALGB (rituximab + methotrexate + cyclophosphosphamide, 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
VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)	Varies	Varies
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituxan® (rituximab)	Varies	Varies
Revlimid® (lenalidomide) + Rituxan® (rituximab)	Varies	Varies
CVP (cyclophosphamide, vincristine, prednisone) + Rituxan® (rituximab)	Varies	Varies
Bendamustine + 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

- Contraindication(s):
  - None

- Boxed Warning(s):
  - None

APPENDIX D: General Information

- Zanubrutinib is a small-molecule inhibitor of BTK. Zanubrutinib forms a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK activity. BTK is a signaling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. In B-cells, BTK signaling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion. In nonclinical studies, zanubrutinib inhibited malignant B-cell proliferation and reduced tumor growth.

References

1. Brukinsa® Prescribing Information. San Mateo, CA; BeiGene USA, Inc: November 2019. Available at www.Brukinsa.com. Accessed February 5, 2021.

2. National Comprehensive Cancer Network. B-cell Lymphomas. Version 2.2021 – February 16, 2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/b-cell_blocks.pdf. Accessed February 16, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.nccn.org.Accessed February 5, 2021
4. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 2.2021 – December 3, 2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed February 16, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	05/07/2020	05/21/2020
Policy was reviewed: 1) Continuation therapy criteria II.A.1. added "listed in this policy" 2) Appendix A Abbreviation/Acronym Key for MCL and BTK added 3) Added Appendic D : General Information 4) References were updated. 5) Added initial therapy approval criteria for CLL/SLL 6) Added Appendix B Therapeutic alternatives drug table	02/16/2021	03/09/2021