Clinical Policy Title:	zanubrutinib
Policy Number:	RxA.620
Drug(s) Applied:	Brukinsa®
Original Policy Date:	05/21/2020
Last Review Date:	10/19/2023
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

A. Mantle Cell Lymphoma (must meet all):

1. Diagnosis of Mantle Cell Lymphoma;
2. Age ≥ 18 years;
3. Member has received at least one prior first line therapy;
4. If disease is positive for BTK C481S mutation: Member has not had previous disease progression on Imbruvica®;
5. Prescribed by or in consultation with an oncologist or a hematologist;
6. Request meets one of the following (a, b, or c):*
   a. Dose does not exceed 320 mg per day;
   b. If co-administered with a moderate CYP3A4 inducer (e.g., bosentan, efavirenz, phenobarbital, primidone), dose does not exceed 640 mg 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: 12 months
Medicaid: 6 months

B. Waldenström's Macroglobulinemia (must meet all):

1. Diagnosis of Waldenström's Macroglobulinemia;
2. Age ≥ 18 years;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Brukinsa® is not prescribed concurrently with Imbruvica® or Calquence®;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 320 mg per day;
   b. If co-administered with a moderate CYP3A4 inducer (e.g., bosentan, efavirenz, phenobarbital, primidone), dose does not exceed 640 mg per day;
   c. 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: 12 months

Medicaid: 6 months

C. Marginal Zone Lymphoma (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;
   c. Nodal MZL;
   d. Splenic MZL;
2. Age ≥ 18 years;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Member has received at least one anti-CD20-based regimen (e.g., bendamustine, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone, ibrutinib);
5. Brukinsa® is not prescribed concurrently with Imbruvica®;
6. Request meets one of the following (a, b or c):*
   a. Dose does not exceed 320 mg per day;
   b. If co-administered with a moderate CYP3A4 inducer (e.g., bosentan, efavirenz, phenobarbital, primidone), dose does not exceed 640 mg per day;
   c. 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: 12 months
Medicaid: 6 months

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

1. Diagnosis of CLL/SLL;
2. Age ≥ 18 years;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Prescribed as single agent therapy;
5. If disease is positive for BTK C481S mutation: Member has not had previous disease progression on Imbruvica;
6. Request meets one of the following (a, b or c):*
   a. Dose does not exceed 320 mg per day;
   b. If co-administered with a moderate CYP3A4 inducer (e.g., bosentan, efavirenz, phenobarbital, primidone), dose does not exceed 640 mg per day;
   c. 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: 12 months
Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria listed in this policy;
2. The member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):*

a. Dose does not exceed 320 mg 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: 12 months
Medicaid: 12 months

References

1. National Comprehensive Cancer Network. B-cell Lymphomas. Version 2.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed March 01, 2023.
2. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 2.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed March 01, 2023.
3. National Comprehensive Cancer Network. Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma. Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed March 01, 2023.

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. References were updated. 3. Added initial therapy approval criteria for CLL/SLL.	02/16/2021	03/09/2021
Policy was reviewed: 1. Initial Approval Criteria I.A.1.c and I.A.1.d updated to remove Nodal marginal zone lymphoma & Splenic marginal zone lymphoma. 2. Initial Approval Criteria I.B Updated to include approval criteria for Waldenström's macroglobulinemia (WM). 3. Initial Approval Criteria I.C Updated to include approval criteria for marginal zone lymphoma (MZL). 4. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 5. References were reviewed and updated.	12/13/2021	01/17/2022
Policy was reviewed: 1. Initial Approval Criteria, I.A.3 and I.C.3: Updated to remove prior contraindication criteria Member is intolerant to or have contraindications to ibrutinib. 2. Initial Approval Criteria, I.B.4 and I.C.5: Updated to include new prescribing criteria Brukinsa® is not prescribed concurrently with Imbruvica®. 3. Initial Approval Criteria, I.B.4.d: Updated to include new criteria pertaining to indication Waldenström's	10/19/2022	01/17/2023

Macroglobulinemia, For the management of symptomatic Bing-Neel syndrome. 4. Initial Approval Criteria, I.D.5: Updated to include new contraindication criteria Member has intolerance or contraindication to other BTK inhibitors (e.g., ibrutinib, acalabrutinib). 5. Continued Therapy Approval, II.A.3: Updated to remove therapy response criteria The prescriber has reassessed efficacy and established goals of therapy. 6. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.A.1: Updated diagnosis criteria from Member has one of the following types of B-cell lymphoma diagnosis: a. Mantle cell lymphoma; b. Gastric MALT Lymphoma; c. Non-gastric MALT lymphoma (non-cutaneous) to Diagnosis of Mantle Cell Lymphoma. 2. Initial Approval Criteria, I.A.4: Updated to include new disease progression criteria If disease is positive for BTK C481S mutation: Member has not had previous disease progression on Imbruvica®. 3. Initial Approval Criteria I.A, I.B, I.C and I.D: Updated Approval Duration criteria for commercial from 6 months to 12 months. 4. Initial Approval Criteria, I.B.4: Updated combination therapy criteria from Brukinsa® is not prescribed concurrently with Imbruvica® to Brukinsa® is not prescribed concurrently with Imbruvica® or Calquence®. 5. Initial Approval Criteria, I.B.5: Updated to remove prior criteria pertaining to indication Waldenström's Macroglobulinemia, " Brukinsa® will be used as single agent for one of the following (a, b, or c): a. For primary therapy; b. Request to be considered for relapse if previously used as primary therapy that was well tolerated and elicited a prolonged response; c. Request is to be used as alternative therapy for previously treated disease that does not respond to primary therapy or for progressive or relapsed disease; d. For the management of symptomatic Bing-Neel syndrome." 6. Initial Approval Criteria, I.C.1: Updated indication from Diagnosis of relapsed or refractory Marginal Zone Lymphoma to Diagnosis of one of the following MZL subtypes (a, b, c, or d): a. Gastric MALT lymphoma;	03/01/2023	04/13/2023

b. Nongastric MALT lymphoma; c. Nodal MZL; d. Splenic MZL; 7. Initial Approval Criteria, I.D: Updated from off label indication to labelled indication. 8. Initial Approval Criteria, I.D.3: Updated to remove prior prescribing criteria “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” 9. Initial Approval Criteria, I.D.4: Updated to include new prescriber criteria Prescribed as single agent therapy. 10. Initial Approval Criteria, I.D.5: Updated to include new disease progression criteria If disease is positive for BTK C481S mutation: Member has not had previous disease progression on Imbruvica. 11. Initial Approval Criteria, I.D.7: Updated to remove prior intolerance criteria “Member has intolerance or contraindication to other BTK inhibitors (e.g., ibrutinib, acalabrutinib).” 12. Continued Therapy Approval: Updated Approval Duration criteria from 6 months to 12 months. 13. References were reviewed and updated.		
Policy was reviewed.	10/19/2023	10/19/2023