Clinical Policy Title:	ibrutinib
Policy Number:	RxA.170
Drug(s) Applied:	Imbruvica®
Original Policy Date:	02/07/2020
Last Review Date:	8/28/2024
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

A. Chronic Graft-Versus-Host Disease (cGVHD) (must meet all)**:**

1. Diagnosis of cGVHD;
2. Member has a history of bone marrow/stem cell transplant;
3. Trial and failure of at least one other systemic therapy (e.g., systemic corticosteroids, immunosuppressants) unless contraindicated or clinically significant adverse effects are experienced;
4. Imbruvica® is not prescribed concurrently with Jakafi® or Rezurock®.

Approval Duration

All Lines of Business (except Medicare): 12 months

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

1. Diagnosis of CLL or SLL;
2. Prescribed as a single agent or in combination with one of the following (a or b):
   a. Rituximab;
   b. Obinutuzumab.

Approval Duration

All Lines of Business (except Medicare): 12 months

C. Waldenstrom's Macroglobulinemia (WM)(must meet all)**:**

1. Diagnosis of WM;
2. Prescribed as a single agent or in combination with rituximab.

Approval Duration

All Lines of Business (except Medicare): 12 months

D. NCCN Compendium Indications (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a, b, or c):
   a. B-cell lymphoma subtype (i, ii, iii, iv, v, vi or vii):
      i. AIDS-related non-germinal center diffuse large B-cell lymphoma (DLBCL);
      ii. High-grade B-cell lymphoma;
      iii. Post-transplant lymphoproliferative disorder (PTLD);
      iv. DLBCL;
      v. Histologic transformation of CLL/SLL to DLBCL;
      vi. Mantle cell lymphoma (MCL);

vii. Marginal zone lymphoma (MZL) of one of the following subtypes (1, 2, 3, or 4):
1. Gastric MALT lymphoma;
2. Nongastric MALT lymphoma (noncutaneous);
3. Nodal MZL;
4. Splenic MZL;

b. Hairy cell leukemia (HCL);
c. Primary CNS lymphoma;

2. Disease is relapsed, recurrent, or progressive.

Approval Duration
All Lines of Business (except Medicare): 12 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**
1. Auto-approval based on lookback functionality within the past 120 days as a proxy for member responding positively to therapy.

Approval Duration
All Lines of Business (except Medicare): 12 months

References

1. National Comprehensive Cancer Network Guidelines. B-cell lymphomas Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed August 28, 2024.
2. National Comprehensive Cancer Network. Hairy Cell Leukemia Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed August 28, 2024.
3. National Comprehensive Cancer Network. Central Nervous System Cancers Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed August 28, 2024.
4. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed August 28, 2024.
5. National Comprehensive Cancer Network. Hematopoietic Cell Transplantation Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf. Accessed August 28, 2024.
6. National Comprehensive Cancer Network. Waldenström Macroglobulinemia/ Lymphoplasmacytic Lymphoma Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed August 28, 2024.
7. Ruutu T, Gratwohl A, De witte T, et al. Prophylaxis and treatment of GVHD: EBMT-ELN working group recommendations for a standardized practice. Bone Marrow Transplant. 2014 Feb;49(2): 168-173. Available at: https://pubmed.ncbi.nlm.nih.gov/23892326/. Accessed August 28, 2024.
8. Lee SJ, Vogelsang G, Flowers ME. Chronic graft-versus-host disease. Biology of Blood and Marrow Transplant 2003; 9:215-233. Available at: https://pubmed.ncbi.nlm.nih.gov/12720215/. Accessed August 28, 2024.
9. Filipovich AH, Weisdorf D, Pavletic S, et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. Diagnosis and Staging Working Group Report. Biol Blood Marrow Transplant. 2005 Dec;11(12):945-956. Available at: https://pubmed.ncbi.nlm.nih.gov/16338616/. Accessed August 28, 2024.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed:	08/03/2020	09/14/2020

1. Policy title table was updated: Clinical Policy Title was updated to "ibrutinib"; Drug(s) Applied was updated to "Imbruvica®"; Line of Business Policy Applies to was updated to "All". 2. Clinical policy was updated: Approval duration was updated for both Initial and Continued Approval Criteria; Continued Approval was rephrased to "Currently receiving medication that has been authorized by RxAdvance…".; Removed preference to capsules over tablets; Updated CLL/SLL and WM criteria to allow combination use per package insert labelling update. 3. References were updated.		
Policy was reviewed: 1. Clinical Policy title was updated. 2. Continued Therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance..." 3. References were updated.	04/13/2021	06/10/2021
Policy was reviewed: 1. Initial Approval Criteria I.A.6.a, I.B.5.a, I.E.5.a: Updated to remove 3 capsules or 1 tablet. 2. Initial Approval Criteria I.C.5.a, I.D.5.a: Updated to remove 4 capsules or 1 tablet. 3. Initial Approval Criteria I.B.4.d : Update to add new criteria For histologic (Richter's) transformation of CLL/SLL to diffuse large B-cell lymphoma (DLBCL), Opdivo® (nivolumab) or Keytruda® (pembrolizumab), 4. References were reviewed and updated.	01/14/2022	04/18/2022
Policy was reviewed: 1. Initial Approval Criteria, I.A.3: Updated age criteria from Member is ≥ 18 years of age to Age ≥ 1 year. 2. Initial Approval Criteria, I.A.5: "Member meets one of the following (a or b): a. Failure of a systemic corticosteroid (e.g., prednisone) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced; b. If there is a intolerance or contraindication to systemic corticosteroids, failure of an immunosuppressant [e.g., mycophenolate mofetil, calcineurin inhibitors (e.g., cyclosporine, tacrolimus), sirolimus] at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experience;" was replaced with Trial and failure of at least one other systemic therapy (e.g., systemic corticosteroids, immunosuppressants) unless contraindicated or	01/18/2023	04/13/2023

clinically significant adverse effects are experienced.

3. Initial Approval Criteria, I.A.6: Updated to include new combination therapy criteria Imbruvica® is not prescribed concurrently with Jakafi® or Rezurock®.
4. Initial Approval Criteria, I.A, I.B, I.C, I.D. I.E and I.F: Updated approval duration criteria from 6 months to 12 months for Commercial.
5. Initial Approval Criteria, I.B.4.c.: Updated to remove prior combination therapy criteria "bendamustine and rituximab".
6. Initial Approval Criteria, I.B.4.d: Updated to remove prior combination therapy criteria "For histologic (Richter's) transformation of CLL/SLL to diffuse large B-cell lymphoma (DLBCL), Opdivo® (nivolumab) or Keytruda® (pembrolizumab)".
7. Initial Approval Criteria, I.C.4.a: Updated combination therapy criteria from Prescribed in combination with rituximab as pre-treatment for HyperCVAD to Prescribed in combination with rituximab as pre-treatment in order to limit the number of cycles of aggressive induction therapy with RHyperCVAD (rituximab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone).
8. Initial Approval Criteria, I.D.1: Updated diagnostic criteria from Diagnosis of MZL to 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.
9. Initial Approval Criteria, I.F.1.a: "Non-Hodgkin's (B-cell) lymphoma or any of its subtypes" was replaced with B-cell lymphoma subtype (i, ii, iii, iv, or v):
    i. AIDS-related non-germinal center DLBCL;
    ii. High-grade B-cell lymphoma;
    iii. Post-transplant lymphoproliferative disorder (PTLD);
    iv. DLBCL;
    v. Histologic transformation of CLL/SLL to DLBCL.
10. Initial Approval Criteria, I.F.5.b: "For CNS lymphoma or non-Hodgkin's (B-cell) lymphoma: Received at least one (1) prior therapy, unless contraindicated or clinically significant adverse effects are experienced to all;" was replaced with "For primary CNS lymphoma, request is for use as either induction therapy or for relapsed or refractory disease."
11. Initial Approval Criteria, I.F.5.c: Updated to include new trial and failure criteria For B-cell lymphoma, received ≥ 1 prior line of systemic therapy, unless contraindicated or clinically significant adverse effects are experienced to all.
12. Initial Approval Criteria, I.F.6.a: Updated to remove prior

dosing criteria "Dose does not exceed FDA prescribing guidelines or dosing is supported by evidence-based guidelines or peer-reviewed literature for the relevant off-label use." 13. Continued Therapy Approval, II.A.3: Updated to include new combination therapy criteria For cGVHD, Imbruvica is not prescribed concurrently with Jakafi or Rezurock. 14. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.C: Updated to remove approval criteria for Mantle Cell Lymphoma. 2. Initial Approval Criteria, I.D: Updated to remove approval criteria for Marginal Zone Lymphoma. 3. Initial Approval Criteria, I.D.1.a.vi, I.D.1.a.vii.1, I.D.1.a.vii.2, I.D.1.a.vii.3, and I.D.1.a.vii.4: Updated to include new diagnosis criteria: i. Mantle cell lymphoma (MCL); ii. Marginal zone lymphoma (MZL) subtype (1, 2, 3, or 4): 1. Gastric MALT lymphoma; 2. Nongastric MALT lymphoma (noncutaneous); 3. Nodal MZL; 4. Splenic MZL; 4. Initial Approval Criteria, I.D.5.c.ii and I.D.5.c.iii: Updated to include new induction and combination therapy criteria: a. For MCL only: Request is for use as either induction therapy or maintenance therapy; b. For MCL only: Prescribed in combination with rituximab as pretreatment in order to limit the number of cycles of aggressive induction therapy with RHyperCVAD (ritixumab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone); 5. References were reviewed and updated.	06/28/2023	07/13/2023
Policy was reviewed.	10/19/2023	10/19/2023
Policy was reviewed: 1. Removed prescriber restrictions. 2. Removed age restrictions. 3. Removed dose restrictions. 4. Updated Continued therapy approval with auto-approval based on lookback functionality within the past 120 days.. 5. Removed other reauthorization requirements including positive response to therapy.. 6. Updated approval duration verbiage. 7. References were reviewed and updated.	08/28/2024	09/13/2024