

Imbruvica® (ibrutinib) (Oral)

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I. Length of Authorization

Coverage will be provided for six months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- Imbruvica 140 mg capsule/tablet: 4 capsules/tablets per day
- Imbruvica 70 mg capsule: 1 capsules per day
- Imbruvica 280 mg tablet: 2 tablets per day
- Imbruvica 560 mg tablet: 1 tablet per day
- Imbruvica 420 mg tablet: 1 tablet per day

B. Max Units (per dose and over time) [Medical Benefit]:

- 560 mg daily

III. Initial Approval Criteria

Coverage for is provided for treatment of the following conditions:

- Patient is 18 years or older; **AND**

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) †

- Used as a single agent; **OR**
- Used in combination with rituximab and bendamustine **OR** in combination with obinutuzumab

Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma (WM/LPL) †

- Used as single agent or in combination with rituximab

Chronic Graft versus Host Disease (cGVHD) †

- Patient is post-allogeneic stem cell transplant (generally 3 or more months); **AND**

- Patient has failed one or more previous lines of systemic therapy for the treatment of cGVHD (e.g., corticosteroids or immunosuppressants such as cyclosporine)

Non-Hodgkin Lymphoma (NHL):

- Used as a single agent for relapsed/refractory or progressive disease as subsequent therapy for one of the following:
 - Marginal Zone Lymphoma (MZL) † (including Nodal and Splenic)
 - Follicular Lymphoma ‡
 - Nongastric MALT Lymphoma ‡
 - Gastric MALT Lymphoma ‡
 - Hairy Cell Leukemia ‡
- AIDS-Related B-cell Lymphoma ‡
 - Used as single agent, subsequent therapy for relapsed disease; **AND**
 - Patients are not candidates for transplant
- Diffuse Large B-Cell Lymphoma ‡
 - Used as a single agent in patients with histologic transformation to Diffuse Large B-cell Lymphoma as subsequent therapy after multiple lines of chemoimmunotherapy for indolent or transformed disease ‡; **OR**
 - Used as subsequent therapy partial response, no response, relapsed, progressive, or refractory non-germinal center disease in noncandidates for transplant
- High-Grade B-Cell Lymphoma ‡
 - Used as subsequent therapy partial response, no response, relapsed, progressive, or refractory disease in noncandidates for transplant
- Mantle Cell Lymphoma (MCL) †
 - Used as subsequent therapy as a single agent or in combination with rituximab; **OR**
 - Used in combination with rituximab as pre-treatment to limit the number of induction therapy cycles ‡
- Post-Transplant Lymphoproliferative Disorders (PTLD) ‡
 - Used as subsequent therapy; **AND**
 - Used for patients with partial response, persistent or progressive disease after receiving first-line chemo-immunotherapy for monomorphic PTLD.
- Primary CNS Lymphoma ‡
 - Used as single agent therapy for relapsed or refractory disease; **AND**
 - Patient has received previous whole brain radiation therapy; **OR**
 - Used in combination with radiation therapy in patients who had either no or a short response to a high-dose methotrexate based regimen without previous radiation therapy; **OR**
 - Patient had a long response (≥ 12 months) to prior high-dose chemotherapy without prior radiation therapy **OR** with stem cell rescue

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s)

IV. Renewal Criteria

Authorizations can be renewed based on the following criteria:

- Patients continues to meet criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: hemorrhage, severe infections, myelosuppression (neutropenia, thrombocytopenia, anemia), atrial fibrillation, tumor lysis syndrome, hypertension, and second primary malignancies, etc.; **AND**

Oncology indications:

- Tumor response with stabilization of disease or decrease in size of tumor or tumor spread

cGVHD:

- Response to therapy with an improvement in one or more of the following:
 - Clinician assessments (e.g., NIH Skin Score, Upper GI Response Score, NIH Lung Symptom Score, etc.)
 - Patient-reported symptoms (e.g., Lee Symptom Scale, etc.)

V. Dosage/Administration

Indication	Dose
DLBCL, MCL, MZL, MALT, PTL, CNS lymphoma, & Hairy Cell Leukemia	560 mg orally once daily until disease progression or unacceptable toxicity
CLL/SLL (single agent or in combination with rituximab and bendamustine or with obinutuzumab)	420 mg orally once daily until disease progression or unacceptable toxicity. <i>*When used in combination with rituximab or obinutuzumab, consider administering Imbruvica prior to therapy, when given on the same day.</i>
WM/LPL (single agent or in combination with rituximab)	420 mg orally once daily until disease progression or unacceptable toxicity
cGVHD	420 mg orally once daily until progression, recurrence of an underlying malignancy, or unacceptable toxicity

VI. Billing Code/Availability Information

HCPCS:

- J8999 - Prescription drug, oral, chemotherapeutic, Not Otherwise Specified
- C9399 - Unclassified drugs or biologicals (Hospital Outpatient Use ONLY)

NDC:

- Imbruvica 140 mg capsule: 57962-0140-xx
- Imbruvica 70 mg capsule: 57962-0070-xx
- Imbruvica 560 mg tablet: 57962-0560-xx

- Imbruvica 420 mg tablet: 57962-0420-xx
- Imbruvica 280 mg tablet: 57962-0280-xx
- Imbruvica 140 mg tablet: 57962-0014-xx

VII. References

1. Imbruvica [package insert]. Horsham, PA; Janssen Biotech, Inc. January 2019. Accessed February 2019.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for ibrutinib. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2019.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for B-Cell Lymphomas. National Comprehensive Cancer Network, 2019. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2019.
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5. Treon SP, Tripsas CK, Yang G, et al. A Prospective Multicenter Study of the Bruton's Tyrosine Kinase Inhibitor Ibrutinib In Patients With Relapsed Or Refractory Waldenstrom's Macroglobulinemia. [abstract]. *Hematol Oncol*. 2013; 31 (suppl 1):119:067.
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7. Lee SJ, Wolff D, Kitko C, et al. Measuring therapeutic response in chronic graft-versus-host disease. National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: IV. The 2014 Response Criteria Working Group report. *Biol Blood Marrow Transplant*. 2015 Jun;21(6):984-99. doi: 10.1016/j.bbmt.2015.02.025.
8. Wilson WH, Young RM, Schmitz R, et al. Targeting B cell receptor signaling with ibrutinib in diffuse large B cell lymphoma. *Nat Med*. 2015 Aug;21(8):922-6.
9. Grommes C, Pastore A, Palaskas N, et al. Ibrutinib Unmasks Critical Role of Bruton Tyrosine Kinase in Primary CNS Lymphoma. *Cancer Discov*. 2017 Sep;7(9):1018-1029.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C83.00	Small cell B-cell lymphoma, unspecified site
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face, and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C83.10	Mantle cell lymphoma, unspecified site
C83.11	Mantle cell lymphoma, lymph nodes of head, face, and neck
C83.12	Mantle cell lymphoma, intrathoracic lymph nodes
C83.13	Mantle cell lymphoma, intra-abdominal lymph nodes
C83.14	Mantle cell lymphoma, lymph nodes of axilla and upper limb
C83.15	Mantle cell lymphoma, lymph nodes of inguinal region and lower limb
C83.16	Mantle cell lymphoma, intrapelvic lymph nodes
C83.17	Mantle cell lymphoma, spleen
C83.18	Mantle cell lymphoma, lymph nodes of multiple sites
C83.19	Mantle cell lymphoma, extranodal and solid organ sites
C83.30	Diffuse large B-cell lymphoma, unspecified site
C83.31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.32	Diffuse large B-cell lymphoma, intrathoracic lymph nodes
C83.33	Diffuse large B-cell lymphoma, intra-abdominal lymph nodes
C83.34	Diffuse large B-cell lymphoma, lymph nodes of axilla and upper limb
C83.35	Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.36	Diffuse large B-cell lymphoma, intrapelvic lymph nodes
C83.37	Diffuse large B-cell lymphoma, spleen
C83.38	Diffuse large B-cell lymphoma, lymph nodes of multiple sites
C83.39	Diffuse large B-cell lymphoma, extranodal and solid organ sites
C83.80	Other non-follicular lymphoma, unspecified site
C83.81	Other non-follicular lymphoma, lymph nodes of head, face and neck
C83.82	Other non-follicular lymphoma, intrathoracic lymph nodes

ICD-10	ICD-10 Description
C83.83	Other non-follicular lymphoma, intra-abdominal lymph nodes
C83.84	Other non-follicular lymphoma, lymph nodes of axilla and upper limb
C83.85	Other non-follicular lymphoma, lymph nodes of inguinal region and lower limb
C83.86	Other non-follicular lymphoma, intrapelvic lymph nodes
C83.87	Other non-follicular lymphoma, spleen
C83.88	Other non-follicular lymphoma, lymph nodes of multiple sites
C83.89	Other non-follicular lymphoma, extranodal and solid organ sites
C83.90	Non-follicular (diffuse) lymphoma, unspecified, unspecified site
C83.91	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of head, face, and neck
C83.92	Non-follicular (diffuse) lymphoma, unspecified, intrathoracic lymph nodes
C83.93	Non-follicular (diffuse) lymphoma, unspecified, intra-abdominal lymph nodes
C83.94	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of axilla and upper limb
C83.95	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of inguinal region and lower limb
C83.96	Non-follicular (diffuse) lymphoma, unspecified, intrapelvic lymph nodes
C83.97	Non-follicular (diffuse) lymphoma, unspecified, spleen
C83.98	Non-follicular (diffuse) lymphoma, unspecified, lymph nodes of multiple sites
C83.99	Non-follicular (diffuse) lymphoma, unspecified, extranodal and solid organ sites
C85.10	Unspecified B-cell lymphoma, unspecified site
C85.11	Unspecified B-cell lymphoma, lymph nodes of head, face, and neck
C85.12	Unspecified B-cell lymphoma, intrathoracic lymph nodes
C85.13	Unspecified B-cell lymphoma, intra-abdominal lymph nodes
C85.14	Unspecified B-cell lymphoma, lymph nodes of axilla and upper limb
C85.15	Unspecified B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.16	Unspecified B-cell lymphoma, intrapelvic lymph nodes
C85.17	Unspecified B-cell lymphoma, spleen
C85.18	Unspecified B-cell lymphoma, lymph nodes of multiple sites
C85.19	Unspecified B-cell lymphoma, extranodal and solid organ sites
C85.20	Mediastinal (thymic) large B-cell lymphoma, unspecified site
C85.21	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of head, face, and neck
C85.22	Mediastinal (thymic) large B-cell lymphoma, intrathoracic lymph nodes
C85.23	Mediastinal (thymic) large B-cell lymphoma, intra-abdominal lymph nodes
C85.24	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of axilla and upper limb
C85.25	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C85.26	Mediastinal (thymic) large B-cell lymphoma, intrapelvic lymph nodes
C85.27	Mediastinal (thymic) large B-cell lymphoma, spleen

ICD-10	ICD-10 Description
C85.28	Mediastinal (thymic) large B-cell lymphoma, lymph nodes of multiple sites
C85.29	Mediastinal (thymic) large B-cell lymphoma, extranodal and solid organ sites
C85.80	Other specified types of non-Hodgkin lymphoma, unspecified site
C85.81	Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face and neck
C85.82	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
C85.83	Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes
C85.84	Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb
C85.85	Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region of lower limb
C85.86	Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes
C85.87	Other specified types of non-Hodgkin lymphoma, spleen
C85.88	Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C88.0	Waldenström macroglobulinemia
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT-lymphoma)
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse
C91.40	Hairy cell leukemia not having achieved remission
C91.42	Hairy cell leukemia, in relapse
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)
D89.811	Chronic graft-versus-host disease
Z85.72	Personal history of non-Hodgkin lymphomas
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: <http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC