Clinical Policy: Ibrutinib (Imbruvica)

Reference Number: CP.PHAR.126
Effective Date: 10/15
Last Review Date: 03/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for ibrutinib (Imbruvica®) capsules for oral use.

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Imbruvica is **medically necessary** when one of the following criteria are met:

I. Initial Approval Criteria

A. Mantle Cell Lymphoma (must meet all)**:**
1. Diagnosis of mantle cell lymphoma (MCL);
2. Member meets one of the following (a or b):
   a. FDA approved use: previously received at least one prior therapy for MCL;
   b. Off-label NCCN recommended use (i and ii):
      i. Age ≥ 65 years;
      ii. Ibrutinib will be used in combination with rituximab as pre-treatment in order to limit the number of cycles of less aggressive induction therapy with RHyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) regimen;
3. Prescribed dose of Imbruvica does not exceed 560 mg per day (4 capsules per day).

Approval duration: 6 months

B. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (must meet all)**:**
1. Diagnosis of chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL);
2. Prescribed dose of Imbruvica does not exceed 420 mg per day (3 capsules per day).

Approval duration: 6 months

C. Waldenström's Macroglobulinemia (must meet all)**:**
1. Diagnosis of Waldenström's macroglobulinemia (WM);
2. Prescribed dose of Imbruvica does not exceed 420 mg per day (3 capsules per day).

Approval duration: 6 months

D. Marginal Zone Lymphoma (must meet all)**:**
1. Diagnosis of marginal zone lymphoma (MZL);

2. Member has received at least one prior anti-CD20-based therapy (e.g., rituximab), unless contraindicated;
3. Prescribed dose of Imbruvica does not exceed 560 mg per day (4 capsules per day).

Approval duration: 6 months

E. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy.
1. Additional Imbruvica uses outlined in the NCCN compendium, and which meet NCCN category 1, 2a, or 2b, are covered for the following indications per the CP.PHAR.57 Global Biopharm Policy:
   a. Non-Hodgkin lymphoma – hairy cell leukemia.

II. Continued Approval

A. All Indications (MCL, CLL/SLL, WM, and MZL)**:**
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Documentation of positive response to therapy (e.g., no disease progression);
3. Prescribed dosage regimen does not exceed the following:
   a. For MCL and MZL: 560 mg per day (4 capsules per day);
   b. For CLL/SLL and WM: 420 mg per day (3 capsules per day).

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:
Ibrutinib is a small-molecule inhibitor of Bruton's tyrosine kinase (BTK). Ibrutinib forms a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK enzymatic activity. BTK is a signaling molecule of the B-cell antigen receptor (BCR) and cytokine receptor pathways. BTK's role in signaling through the B-cell surface receptors results in activation of pathways necessary for B-cell trafficking, chemotaxis, and adhesion. Nonclinical studies show that ibrutinib inhibits malignant B-cell proliferation and survival in vivo as well as cell migration and substrate adhesion in vitro.

Formulations:
Imbruvica is available as 140 mg capsules for oral administration.

FDA Approved Indications:
Imbruvica is a kinase inhibitor/oral capsule formulation indicated for the treatment of patients with:
- MCL who have received at least one prior therapy
- CLL/SLL

- CLL/SLL with 17p deletion
- WM
- MZL who require systemic therapy and have received at least one prior anti-CD20-based therapy

Appendices

Appendix A: Abbreviation Key

BCR: B-cell antigen receptor
BTK: Bruton's tyrosine kinase
CLL: chronic lymphocytic leukemia
MCL: mantle cell lymphoma
MZL: marginal zone lymphoma
SLL: small lymphocytic lymphoma
WM: Waldenström's macroglobulinemia

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
Policy developed	09/15	09/15
Changed 'and' to 'or' in I.E.1 per package insert Updated disclaimer language	01/16	
Policy converted to new template. Removed age and prescriber specialty requirements. Removed question related to moderate or severe hepatic impairment as it is not listed as a contraindication per PI. Added maximum dosage requirement for MCL, CLL/SLL, and WM. Modified CLL/SLL criteria to allow use of Imbruvica as first line therapy for members without 17p deletion per PI and NCCN compendium. Added disease progression or unacceptable toxicity to reasons to discontinue per PI.	07/16	10/16
Added new FDA approved indication: MZL. MCL: added off-label use per NCCN compendium. CLL/SLL: removed "with or without 17p deletion" as that has no impact on coverage. Other diagnoses/indications: added hairy cell leukemia per NCCN compendium. Continued approval: Removed reasons to discontinue. Added requirement for documentation of positive response to therapy.	03/17	03/17

References

1. Imbruvica Prescribing Information. Sunnyvale, CA: Pharmacyclics LLC; January 2017. Available at: https://www.imbruvica.com/. Accessed March 14, 2017.

2. Ibrutinib. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed March 14, 2017.
3. B-cell lymphomas (Version 2.2017). In: National Comprehensive Cancer Network Guidelines. Available at www.NCCN.org. Accessed March 14, 2017.

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.