BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
ORIGINAL EFFECTIVE DATE:	**1/01/2016**
LAST REVIEW DATE:	**2/17/2022**
LAST CRITERIA REVISION DATE:	**2/17/2022**
ARCHIVE DATE:	

IMBRUVICA® (ibrutinib) oral capsule and tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. **All requested data must be provided.** Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy**: Imbruvica (ibrutinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in the patient's diagnosis or is in consultation with an Oncologist, Gastroenterologist, AIDS/HIV Specialist, or Transplant Specialist depending upon indication or use

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:
     a. Mantle cell lymphoma (MCL) who have received at least one prior therapy

     b. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) with or without 17p deletion

     c. Waldenström's macroglobulinemia (WM)

     d. Marginal zone lymphoma (MZL) who require systemic therapy and have received at least one prior anti-CD20-based therapy

     e. Chronic graft-versus-host disease (cGVHD) after failure of one or more lines of systemic therapy

     f. Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

  4. **ALL** of the following baseline tests have been completed before initiation of treatment:
     a. Negative pregnancy test in a woman of childbearing age
     b. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-2

  5. Individual does not have severe hepatic impairment (Child-Pugh Class C)

  6. There are no significant interacting drugs

  Initial approval duration: 6 months

- **Criteria for continuation of coverage (renewal request):** Imbruvica (ibrutinib) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual continues to be seen by a physician specializing in the patient's diagnosis or is in consultation with an Oncologist, Gastroenterologist, AIDS/HIV Specialist, or Transplant Specialist depending upon indication or use

  2. Individual's condition has responded while on therapy

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a. Response is defined as:
   i. Documented evidence of efficacy, disease stability and/or improvement
   ii. No evidence individual has developed any significant unacceptable adverse drug reactions that may exclude continued use

3. Individual has been adherent with the medication

4. Individual has not developed any significant adverse drug effects that may exclude continued use
   a. Significant adverse effect such as:
      i. Life-threatening hemorrhage that persists or recurs after two dose modifications
      ii. Severe or life-threatening cytopenias that persist or recur after two dose modifications
      iii. Severe cardiac arrhythmia hat persists or recurs after two dose modifications
      iv. Tumor Lysis Syndrome (TLS)

5. Individual does not have severe hepatic impairment (Child-Pugh Class C)

6. There are no significant interacting drugs

Renewal duration: 12 months

- Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. **Off-Label Use of Non-cancer Medications**

2. **Off-Label Use of Cancer Medications**

Description:

Imbruvica (ibrutinib) is an inhibitor of Bruton's tyrosine kinase (BTK). Imbruvica (ibrutinib) is indicated for the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy; for the treatment of chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL); for the treatment of chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) with 17p deletion; for the treatment of Waldenström macroglobulinemia (WM); for the treatment of marginal zone lymphoma (MZL) for individuals that require systemic therapy when at least one prior anti-CD20-based therapy has been used; and for chronic graft versus host disease (cGVHD) after failure of one or more lines of system therapy.

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*.

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Resources:

Imbruvica (ibrutinib) product information, revised by Pharmacyclics, LLC. 10-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed December 03, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): B-Cell Lymphomas Version 5.2021 – Updated September 22, 2021. Available at https://www.nccn.org. Accessed December 303, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 1.2022 – Updated September 08, 2021. Available at https://www.nccn.org. Accessed December 02, 2021.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma Version 1.2022– Updated June 24, 2021. Available at https://www.nccn.org. Accessed December 02, 2021.

Chao NJ, Zeiser R. Treatment of acute graft-versus-host disease. In: UpToDate, Negrin RS, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed December 03, 2021.

Zeiser R. Treatment of chronic graft-versus-host disease. In: UpToDate, Negrin RS, Chao NJ, Rosmarin AG (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at http://uptodate.com. Accessed December 03, 2021.

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.