BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINES	
SECTION: DRUGS	
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VENCLEXTA™ (venetoclax)

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:** Venclexta (venetoclax) 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

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis of **ONE** of the following:
     a. Acute myeloid leukemia (AML) in combination with azacitidine or decitabine, or low dose cytarabine for treatment of newly diagnosed adults 75 years or older, or adults who have comorbidities that preclude use of intense induction therapy

     b. Chronic lymphocytic leukemia (CLL) or Small lymphocytic lymphoma (SLL)

     c. 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. Individual has a concurrent prescription for allopurinol and hydration for prophylaxis of tumor lysis syndrome (TLS) before the first dose is administered

  5. **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 0-3

  6. There are no significant interacting drugs

  7. Individual is not to receive live attenuated vaccine(s) prior to, during, or after treatment, unless B-cells have recovered

  Initial approval duration:
  Starting Pack for 5-week initial ramp-up phase, then maintenance dose for 5 months

- **Criteria for continuation of continuation of coverage (renewal request):** Venclexta (venetoclax) 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

  2. Individual's condition responded while on therapy
     a. Response is defined as:
        i. No evidence of disease progression

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

5. Individual has not received live attenuated vaccine(s) prior to, during, or after treatment, unless B-cells have recovered

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:

Venclexta (venetoclax) is indicated for the treatment of patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), with or without 17p deletion, who have received at least one prior therapy.

CLL/SLL are different expressions of the same disease and are managed in the same way. CLL/SLL is characterized by progressive accumulation of small, mature lymphocytic leukemia cells in the peripheral blood, bone marrow, and lymphoid tissue. In CLL the abnormal lymphocytes are predominantly found in the blood, while in SLL the bulk is found in the lymph nodes, bone marrow, and other lymphoid tissues

Several recurring lesions have been identified to have prognostic relevance. Deletions in chromosomes 13q, 17p, and 11q; and trisomy 12 are recognized as negative prognostic factors of the disease affecting prognosis and drug resistance. The 17p deletion is associated with poor outcomes that include a short treatment-free interval, short survival (median survival of 32 months), and poor response to chemotherapy. This deletion is more common in patients who have received prior therapy. Choice of therapy is made based on prognosis, age, comorbid conditions, and cytogenetic abnormalities.

CLL is a lymphoproliferative disorder that accounts for 30% of adult leukemia and 25% of non-Hodgkin lymphoma (NHL); it is a heterogeneous disease with an extremely variable course. It is the most prevalent adult leukemia in Western countries with a median age of diagnosis of 71 years of age.
CLL is characterized by high-level expression of B-cell lymphoma-2 (BCL-2) protein in all patients. It has been well documented that BCL-2 plays a role in cellular apoptosis and is a target for drug therapy. The BCL-2

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protein is a major apoptotic regulator. The ability to nullify the death signal in cancer cells is a key hallmark of cancer. BCL-2 plays a major role in tumor genesis and chemotherapy resistance.

Because there is no cure for CLL, choice of therapy is made based on prognosis, age, and comorbid conditions.

Venclexta (venetoclax) is a selective inhibitor of BCL-2 protein, an anti-apoptotic protein. It helps restore the process of apoptosis by binding directly to the BCL-2 protein inhibiting the effects of BCL-2. Venclexta (venetoclax) promotes apoptosis or cell death by restoring normal cell death pathways within cancerous B-cells. Venclexta (venetoclax) is the second targeted oral agent for CLL with the 17p deletion. Imbruvica (ibrutinib) was approved for CLL with the 17p deletion in July 2014.

Resources:

Venclexta (venetoclax) product information, revised by AbbVie, Inc. 12-2021. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed May 13, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Myeloid Leukemia Version 1.2022 – Updated December 02, 2021. Available at https://www.nccn.org. Accessed May 13, 2022.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 2.2022 – Updated January 18, 2022. Available at https://www.nccn.org. Accessed May 13, 2022.

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.