BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

VENCLEXTA™ (venetoclax) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for VENCLEXTA (venetoclax)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with an Oncologist

Indication
- Acute myeloid leukemia (AML) in combination with azacitidine or decitabine, or low dose cytarabine for newly diagnosed adults 75 years or older, or adults with comorbidities that preclude use of intense induction therapy
- Chronic lymphocytic leukemia (CLL) or Small lymphocytic lymphoma (SLL)

ORIGINAL EFFECTIVE DATE: 05/19/2016 | ARCHIVE DATE: | LAST REVIEW DATE: 05/15/2025 | LAST CRITERIA REVISION DATE: 05/16/2024

- Other oncologic direct treatment use listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

Age Requirement
- 18 years or older

Baseline Clinical Evaluation
- Negative pregnancy test in a woman of childbearing age
- Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 3

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the U.S. Food and Drug Administration (FDA)

Safety
- No concomitant use of strong (per FDA label) CYP3A inhibitors at initiation and during ramp-up phase in CLL/SLL (e.g., ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin, clarithromycin, etc.)
- No concomitant use of moderate or strong CYP3A inducers (e.g., armodafinil, bexarotene, bosentan, rifampin, rifabutin, phenobarbital, carbamazepine, etc.)
- No live attenuated vaccines prior to, during, or after treatment unless B-cells have recovered
- Concurrent prescription for allopurinol and hydration for prophylaxis of tumor lysis syndrome before first dose

Documentation Requirements
- A completed request form must be submitted, including:
  - Chart notes that include the individual has a concurrent prescription for allopurinol and hydration for prophylaxis of tumor lysis syndrome (TLS) before the first dose is administered
  - Lab results (pregnancy test, ECOG status)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- Starting Pack for 5-week initial ramp-up phase, then maintenance dose for 5 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy)
Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

Prescriber Qualifications
- Continues to be seen by a physician specializing in or in consultation with an Oncologist

PHARMACY COVERAGE GUIDELINE

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Clinical Response
- No evidence of disease progression or unacceptable toxicity

Adherence
- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria
- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- No significant drug-drug interactions or contraindications
- No use of strong CYP3A inhibitors or inducers
- No live attenuated vaccines unless B-cells have recovered
- No concomitant use of strong (per FDA label) CYP3A inhibitors at initiation and during ramp-up phase in CLL/SLL (e.g., ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin, clarithromycin, etc.)
- No concomitant use of moderate or strong CYP3A inducers (e.g., armodafinil, bexarotene, bosentan, rifampin, rifabutin, phenobarbital, carbamazepine, etc.)
- No live attenuated vaccines prior to, during, or after treatment unless B-cells have recovered

Documentation Requirements
- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use

Continuation Therapy Criteria Approval Duration
- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

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

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Description:

Venclexta (venetoclax) is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma. Venclexta (venetoclax) is also indicated in combination with azacitidine, or decitabine, or low dose cytarabine for the treatment of newly diagnosed acute myeloid leukemia (AML) in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.

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 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.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

ECOG Performance status:

Eastern Co-operative Oncology Group (ECOG) Performance Status	
Grade	ECOG description
0	Fully active, able to carry on all pre-disease performance without restriction

1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work
2	Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours
3	Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours
4	Completely disabled. Cannot carry on any self-care. Totally confined to bed or chair
5	Dead
Oken, M.M., Creech, R.H., Tormey, D.C., Horton, J., Davis, T.E., McFadden, E.T., Carbone, P.P.: Toxicity And Response Criteria Of The Eastern Cooperative Oncology Group. Am J Clin Oncol 5:649-655, 1982	

NCCN recommendation definitions:

Category 1:
Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A:
Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B:
Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3:
Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate

Resources:

Venclexta (venetoclax) product information, revised by AbbVie, Inc. 07-2024. Available at DailyMed http://dailymed.nlm.nih.gov. Accessed February 21, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Acute Myeloid Leukemia Version 2.2025 – Updated January 27, 2025. Available at https://www.nccn.org. Accessed April 19, 2025.

National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 3.2025 – Updated April 02, 2025. Available at https://www.nccn.org. Accessed April 19, 2025.

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.