

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 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.

Criteria:

- **Criteria for initial therapy:** Venclexta (venetoclax) and/or generic equivalent (if available) is considered **medically necessary** and will be approved when **ALL** 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. Individual has 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

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

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

PHARMACY COVERAGE GUIDELINE

VENCLEXTA™ (venetoclax) Generic Equivalent (if available)

- 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. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))
6. Individual has received and completed **ALL** the following **baseline tests** before initiation of treatment and with continued monitoring of the individual as clinically appropriate:
 - a. Negative pregnancy test in a woman of childbearing age
 - b. Eastern Cooperative Oncology Group (ECOG) Performance Status of 0-3
7. Individual is not using contraindicated per FDA label strong CYP3A inhibitor at initiation and during the ramp-up phase in patients with CLL/SLL (e.g., ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin, clarithromycin, others)
8. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as use with moderate or strong CYP3A inducers (e.g., armodafinil, bexarotene, bosentan, rifampin, rifabutin, phenobarbital, carbamazepine, others)
9. 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 coverage (renewal request):** Venclexta (venetoclax) and/or generic equivalent (if available) is considered **medically necessary** and will be approved when **ALL** the following criteria are met (**samples are not considered for continuation of therapy**):

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 has responded while on therapy with response defined as there is no evidence of disease progression or unacceptable toxicity
3. Individual has been adherent with the medication
4. **If available:** Individual has failure after adequate trial, contraindication per FDA label, intolerance, or is not a candidate for a **generic equivalent** [Note: Failure, contraindication or intolerance to the generic should be reported to the FDA] ([see Definitions section](#))

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

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

PHARMACY COVERAGE GUIDELINE

VENCLEXTA™ (venetoclax) Generic Equivalent (if available)

5. Individual is not using contraindicated per FDA label strong CYP3A inhibitor at initiation and during the ramp-up phase in patients with CLL/SLL (e.g., ketoconazole, itraconazole, posaconazole, voriconazole, telithromycin, clarithromycin, others)
6. Individual is not currently taking any other drugs which cause severe adverse reactions or any drug interactions requiring discontinuation such as use with moderate or strong CYP3A inducers (e.g., armodafinil, bexarotene, bosentan, rifampin, rifabutin, phenobarbital, carbamazepine, others)
7. Individual has not received live attenuated vaccine(s) prior to, during, or after treatment, unless B-cells have recovered

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 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

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

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

PHARMACY COVERAGE GUIDELINE

VENCLEXTA™ (venetoclax) Generic Equivalent (if available)

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



An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

VENCLEXTA™ (venetoclax) Generic Equivalent (if available)

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.

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

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.