BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 5/19/16**
SECTION: DRUGS	**LAST REVIEW DATE: 5/16/19**
	LAST CRITERIA REVISION DATE: 5/16/19
	ARCHIVE DATE:

VENCLEXTA™ (venetoclax) oral 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.**

VENCLEXTA™ (venetoclax) oral tablet (cont.)

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 an Oncologist
2. Individual is 18 years of age or older
3. A confirmed diagnosis of **ONE** of the following:
   - Chronic lymphocytic leukemia/Small lymphocytic lymphoma (CLL/SLL), with or without 17p deletion in an individual who has received at least one prior therapy as a single agent therapy or with rituximab for relapsed or refractory disease in patients who have indications for treatment
   - Acute myeloid leukemia (AML) in combination with decitabine, azacitidine, or low-dose cytarabine for treatment of newly diagnosed adults who have comorbidities that preclude use of intense induction therapy **or** for post-remission therapy following response to previous lower intensity therapy with the same regimen **or** for relapsed/refractory disease as a component of repeating the initial successful induction regimen if late relapse (≥ 12 months)
   - B-cell Lymphoma – Mantle cell lymphoma as second-line single agent therapy for stage I-IV to achieve a complete response after a partial response to induction therapy **or** for relapse or progressive disease following a response to prior chemoimmunotherapy
   - 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:
   - Comprehensive metabolic panel, with pre-existing abnormalities in serum potassium, uric acid, phosphorus, and calcium are corrected prior to initiation of therapy
   - Complete blood count with differential
   - Negative pregnancy test in a woman of child bearing age
6. There are **NO** contraindications
7. There are no significant interacting drugs
8. Individual is not to receive live attenuated vaccine(s) prior to, during, or after treatment, unless B-cells have recovered
9. Will not be used in an individual with severe hepatic impairment (total bilirubin > 3x ULN)
10. Will not be used in an individual with severe renal impairment (CrCl < 30 mL/min) or individual on dialysis

VENCLEXTA™ (venetoclax) oral tablet (cont.)

Initial approval duration:
Starting Pack for 5 weeks 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 an Oncologist
2. Individual's cancer responded or has not worsened while on therapy
3. Individual has been adherent with the medication
4. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
    - Contraindications as listed in the criteria for initial therapy section
    - Significant adverse effect such as:
        - Tumor Lysis Syndrome
        - Neutropenia
5. Individual does not have severe hepatic impairment (total bilirubin > 3x ULN)
6. Individual does not have severe renal impairment (CrCl < 30 mL/min) or on dialysis
7. There are no significant interacting drugs

Renewal duration: 12 months

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 leukemic 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

VENCLEXTA™ (venetoclax) oral tablet (cont.)

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.

Resources:

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.

Venclexta. Package Insert. Revised by manufacturer 4/2016. Accessed 03-21-2017.

Venclexta. Package Insert. Revised by manufacturer 4/2016. Accessed 05-17-2016.

Venclexta. Package Insert. Revised by manufacturer 12/2017. Accessed 04-18-2018.

Venclexta. Package Insert. Revised by manufacturer 06/2018. Accessed 09-09-2018.

NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 5.2018, Mar 26, 2018. https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf

NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 1.2019, Aug 9, 2018. https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf

Venclexta (venetoclax) product information accessed 03-22-19 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b118a40d-6b56-cee3-10f6-ded821a97018

NCCN Compendium: Venclexta (venetoclax) accessed 03-22-19

BlueCross BlueShield of Arizona

An Independent Licensee of the Blue Cross and Blue Shield Association

Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:		Dosage Form:
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

BlueCross BlueShield of Arizona

An Independent Licensee of the Blue Cross and Blue Shield Association

Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.