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5.21.005

Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Antineoplastic Agents	**Original Policy Date:**	April 29, 2016
Subject:	Venclexta	**Page:**	1 of 6

Last Review Date: March 7, 2025

Venclexta

Description

Venclexta (venetoclax)

Background
Venclexta is used for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). Venclexta is FDA-approved treatment that targets the B-cell lymphoma 2 (BCL-2) protein, which supports cancer cell growth (1).

Regulatory Status
FDA-approved indications: Venclexta is a BCL-2 inhibitor indicated: (1)

1. For the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
2. In combination with azacitidine or decitabine or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy

Off-Label Uses: (2-7)

1. Mantle cell lymphoma (MCL)
2. Acute myeloid leukemia (AML)
3. Waldenstrom macroglobulinemia (WM)
4. Systemic light chain amyloidosis (SLCA)

Venclexta can cause rapid reduction in tumor and thus poses a risk for Tumor Lysis Syndrome (TLS), which can occur within 6-8 hours after the first infusion. Patients with high tumor burden and/or high circulating lymphocyte count are at greater risk for TLS and should receive

appropriate tumor lysis prophylaxis with anti-hyperuricemics (e.g., allopurinol) and hydration beginning 12-24 hours prior to the infusion of Venclexta. For treatment of TLS, correct electrolyte abnormalities, monitor renal function, and fluid balance, and administer supportive care, including dialysis as indicated (1).

Neutropenia may occur during Venclexta therapy. Complete blood counts (CBC) should be monitored throughout the treatment period. Dosing should be interrupted or reduced for severe neutropenia (1).

Venclexta may cause embryo-fetal harm when administered to a pregnant woman. Females of reproductive potential should be advised to avoid pregnancy during treatment. Pregnant patients should be advised of the potential hazard to the fetus (1).

The safety and efficacy of immunization with live or attenuated viral vaccines during or following Venclexta therapy has not been studied. Immunization with live virus vaccines is not recommended during treatment and until B-cell recovery (1).

The safety and effectiveness of Venclexta in pediatric patients have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Venclexta may be considered **medically necessary** if the conditions indicated below are met.

Venclexta may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)

2. Mantle cell lymphoma (MCL)
    a. Patient has received at least **ONE** prior therapy

3. Relapsed or refractory acute myeloid leukemia (AML)

4. Newly-diagnosed acute myeloid leukemia (AML)

    AND ALL of the following:
    a. 75 years or older **OR** have comorbidities that preclude use of intensive induction chemotherapy
    b. Used in combination with azacitidine **OR** decitabine **OR** low-dose cytarabine

5. Waldenstrom macroglobulinemia (WM)
    a. Patient has received at least **ONE** prior therapy

6. Systemic light chain amyloidosis (SLCA)

AND ALL of the following for **ALL** indications:
a. Prescriber agrees to monitor complete blood count (CBC) for neutropenia
b. Prescriber agrees to advise female patients of childbearing potential to avoid pregnancy during treatment

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnoses

Patient must have the following:

1. Chronic lymphocytic leukemia (CLL)
2. Small lymphocytic lymphoma (SLL)
3. Mantle cell lymphoma (MCL)

4. Acute myeloid leukemia (AML)
5. Waldenstrom macroglobulinemia (WM)
6. Systemic light chain amyloidosis (SLCA)

AND ALL of the following for **ALL** indications:

a. **NO** disease progression or unacceptable toxicity
b. Prescriber agrees to monitor complete blood count (CBC) for neutropenia
c. Prescriber agrees to advise female patients of childbearing potential to avoid pregnancy during treatment

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Duration 24 months

Rationale

Summary

Venclexta is used for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). Venclexta is also approved for use in relapsed or refractory acute myeloid leukemia (AML) or newly-diagnosed AML. Venclexta may be used off-label for mantle cell lymphoma (MCL), Waldenstrom macroglobulinemia (WM), and systemic light chain amyloidosis (SLCA). Venclexta can cause rapid reduction in tumor and thus poses a risk for Tumor Lysis Syndrome (TLS), which can occur within 12-24 hours after the first infusion. The safety and efficacy of immunization with live or attenuated viral vaccines during or following Venclexta therapy has not been studied. The safety and efficacy of Venclexta in pediatric patients has not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Venclexta while maintaining optimal therapeutic outcomes.

References

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4. NCCN Clinical Practice Guidelines in Oncology® Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma (Version 2.2025). National Comprehensive Cancer Network, Inc. December 2024. Accessed on January 14, 2025.
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6. Konopleva M, Pollyea DA, Potluri J, et al. Efficacy and Biological Correlates of Response in a Phase II Study of Venetoclax Monotherapy in Patients with Acute Myelogenous Leukemia. Cancer Discovery. 2016 Oct; 6 (10): 1106 - 1117.
7. DiNardo CD, Pratz KW, Letai A, et al. Safety and preliminary efficacy of venetoclax with decitabine or azacitidine in elderly patients with previously untreated acute myeloid leukemia: a non-randomised, open-label, phase 1b study. Lancet Oncology. 2018 Feb; 19 (2): 216 - 228.

Policy History

Date	Action
April 2016	Addition to PA
June 2016	Annual review
September 2016	Annual review
June 2017	Annual review and reference update
June 2018	Annual editorial review and reference update Addition of “at least” to initiation criteria, patient must try and fail “at least” one prior CLL therapy per package insert Removal of the 17P deletion from the CLL diagnosis requirement Addition of AML & MCL diagnoses

November 2018	Addition of new indication: Newly-diagnosed acute myeloid leukemia (AML). Addition of pregnancy warning requirement and monitoring CBC requirement
March 2019	Annual review and reference update
May 2019	Removed requirement of trial of one prior therapy for CLL and SLL
June 2019	Annual review
June 2020	Annual review and reference update
December 2021	Annual review and reference update
December 2022	Annual review and reference update. Changed policy number to 5.21.005. Per reconsideration review, added new diagnoses Waldenstrom macroglobulinemia (WM) and systemic light chain amyloidosis (SLCA)
March 2023	Annual review and reference update
March 2024	Annual review and reference update
March 2025	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.