DRUG QUANTITY MANAGEMENT POLICY – PER RX

POLICY: Oncology – Venclexta Drug Quantity Management Policy – Per Rx
- Venclexta® (venetoclax tablets – AbbVie and Genentech)

REVIEW DATE: 04/19/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Venclexta, a B-cell lymphoma-2 inhibitor, is indicated in adults for the following uses:[1]

- **Acute myeloid leukemia (AML)**, in combination with azacitidine or decitabine or low-dose cytarabine for newly diagnosed AML in adults ≥ 75 years of age or who have comorbidities that preclude use of intensive induction chemotherapy.
- **Chronic lymphocytic leukemia (CLL)**.
- **Small lymphocytic lymphoma (SLL)**.

Dosing

Table 1. Venclexta Recommended Dosing.[1]

Indication	Dosing
CLL/SLL	Venclexta dosing begins with a 5 week ramp-up: • Week 1: 20 mg orally QD • Week 2: 50 mg orally QD • Week 3: 100 mg orally QD • Week 4: 200 mg orally QD • Week 5 and beyond: 400 mg orally QD
	In combination with Gazyva® (obinutuzumab intravenous infusion): • On Cycle 1 Day 22, start Venclexta according to the 5-week ramp-up dosing schedule. After completing the ramp-up phase on Cycle 2 Day 28, continue

	Venclexta 400 mg orally QD from Cycle 3 Day 1 until the last day of Cycle 12.
	In combination with rituximab: • Start the 5-week ramp-up Venclexta dosing schedule, and continue Venclexta 400 mg orally QD for 24 months from Cycle 1 Day 1 of rituximab. Rituximab should be started after completion of the 5-week ramp-up of Venclexta and 7 days of Venclexta 400 mg QD.
	Monotherapy: • Venclexta 400 mg QD after completion of the 5-week ramp-up dosing schedule. Continue until disease progression or unacceptable toxicity.
AML	Venclexta dosing begins with a 3-or 4-day ramp-up: Day 1: 100 mg orally QD Day 2: 200 mg orally QD Day 3: 400 mg orally QD Days 4 and beyond: • Venclexta in combination with azacitidine or decitabine: 400 mg orally QD of each 28-day cycle • Venclexta in combination with low-dose cytarabine: 600 mg orally QD of each 28-day cycle Continue Venclexta, in combination with azacitidine or decitabine or low-dose cytarabine, until disease progression or unacceptable toxicity.

CLL – Chronic lymphocytic leukemia; SLL – Small lymphocytic lymphoma; QD – Once daily; AML – Acute myeloid leukemia.

Off-Label Use

Mantle Cell Lymphoma

Doses ranging from 200 mg/day up to 1,200 mg/day were used in clinical studies; 600 mg/day was a commonly used dose.[2-5,9]

Multiple Myeloma

Doses ranging from 300 mg/day up to 1,200 mg/day were used in clinical studies; 800 mg/day was a commonly used dose.[6-8]

Systemic Light Chain Amyloidosis

Doses ranging from 100 mg/day up to 800 mg/day were used in a clinical trial of Venclexta for systemic light chain amyloidosis.[10]

Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma

In one clinical trial of Venclexta in patients with Waldenström macroglobulinemia, patients received orally 200 mg once daily (QD) for 1 week, followed by 400 mg QD for 1 week, and then 800 mg QD for 2 years.[11]

Availability

Table 2. Venclexta Availability.[1]

Package Size	Package Contents
CLL/SLL Starting Pack	Each pack contains four weekly wallet blister packs: • Week 1 (14 x 10 mg tablets) • Week 2 (7 x 50 mg tablets) • Week 3 (7 x 100 mg tablets) • Week 4 (14 x 100 mg tablets)
Wallet of 10 mg tablets	14 x 10 mg tablets
Wallet of 50 mg tablets	7 x 50 mg tablets
Blister of 10 mg tablets	2 x 10 mg tablets

Blister of 50 mg tablet	1 x 50 mg tablet
Blister of 100 mg tablet	1 x 100 mg tablet
Bottle of 100 mg tablets	28 x 100 mg tablets
	120 x 100 mg tablets
	180 x 100 mg tablets

CLL – Chronic lymphocytic leukemia; SLL – Small lymphocytic lymphoma.

POLICY STATEMENT

This Drug Quantity Management program has been developed to promote the safe, effective, and economic use of Venclexta. If the Drug Quantity Management rule is not met for the requested medication at the point of service, coverage will be determined by the Criteria below. All approvals are provided for 1 year in duration.

Drug Quantity Limits

Product	Package Size/Strength	Retail Maximum Quantity per Rx	Home Delivery Maximum Quantity per Rx
Venclexta® (venetoclax tablets)	CLL/SLL Starting Pack	42 tablets (1 pack)	42 tablets (1 pack)
	Wallet of 10 mg tablets	56 tablets (4 wallets)	168 tablets (12 wallets)
	Wallet of 50 mg tablets	28 tablets (4 wallets)	84 tablets (12 wallets)
	Blister of 10 mg tablets	56 tablets (28 blisters)	168 tablets (84 blisters)
	Blister of 50 mg tablets	28 tablets (28 blisters)	84 tablets (84 blisters)
	100 mg tablets (blisters and bottles)	180 tablets	540 tablets

CLL – Chronic lymphocytic leukemia; SLL – Small lymphocytic lymphoma

Oncology – Venclexta Drug Quantity Management Policy – Per Rx product(s) is(are) covered as medically necessary when the following criteria is(are) met. Any other exception is considered not medically necessary.

CRITERIA

Venclexta 10 mg and 50 mg tablets

No overrides recommended.

Venclexta 100 mg tablets

1. If the patient has multiple myeloma, systemic light chain amyloidosis, or Waldenström macroglobulinemia/lymphoplasmacytic lymphoma, approve the requested quantity, not to exceed 240 tablets per dispensing at retail or 720 tablets per dispensing at home delivery.

REFERENCES

1. Venclexta® tablets [prescribing information]. North Chicago, IL and South San Francisco, CA: AbbVie and Genentech; June 2022.
2. Eyre TA, Walter HS, Iyengar S, et al. Efficacy of venetoclax monotherapy in patient with relapsed, refractory mantle cell lymphoma after Bruton tyrosine kinase inhibitor therapy. *Haematologica*. 2019;104:e68-e71.
3. Zhao S, Kanagal-Shamanna R. Navsaria L, et al. Efficacy of venetoclax in high risk relapsed mantle cell lymphoma (MCL) – outcomes and mutation profile from venetoclax resistant MCL patients. *Am J Hematol.* 2020; 95:623-629.
4. Tam CS, Anderson MA, Pott C, et al. Ibrutinib plus venetoclax for the treatment of mantle-cell lymphoma. *N Eng J Med.* 2018;378:1211-1233.
5. Wang M, Ramchandren R, Chen R, et al. Concurrent ibrutinib plus venetoclax in relapsed/refractory mantle cell lymphoma: the safety run-in of the phase 3 SYMPATICO study. *J Hematol Oncol.* 2021;14(1):179.
6. Kumar SK, Harrison SJ, Cavo M, et al. Venetoclax or placebo in combination with bortezomib and dexamethasone in patients with relapsed or refractory multiple myeloma (BELLINI): a randomised, double-blind, multicentre, phase 3 trial. *Lancet Oncol.* 2020;21(12):1630-1642.
7. Kumar SK, Kaufman JL, Gasparetto C, et al. Efficacy of venetoclax as targeted therapy for relapsed/refractory t(11;14) multiple myeloma. *Blood.* 2017;130(22):2401-2409.
8. Basali D, Chakraborty R, Rybicki L, et al. Real-world data on safety and efficacy on venetoclax-based regimens in relapsed/refractory t(11;14) multiple myeloma. *Br J Haematol*. 2020;189(6):1136-1140.
9. Portell CA, Wages NA, Kahl BS, et al. Dose-finding study of ibrutinib and venetoclax in relapsed or refractory mantle cell lymphoma. *Blood Adv*. 2022;6(5):1490-1498.
10. Premkumar VJ, Lentzsch S, Pan S, et al. Venetoclax induces deep hematologic remissions in T(11;14) relapsed/refractory AL amyloidosis. *Blood Cancer J*. 2021;11(1):10.
11. Castillo JJ, Allan JN, Siddiqi T, et al. Venetoclax in previously treated Waldenström macroglobulinemia. *J Clin Oncol*. 2022;40(1):63-71.

History

Type of Revision	Summary of Changes	Review Date
Annual Revision	Policy was updated to reflect the existing quantity limits when a product is obtained via home delivery. **CLL/SLL Starting Pack:** Home delivery quantity limit was changed from 126 tablets (3 packs) to 42 tablets (1 pack) per dispensing.	03/22/2023
Annual Revision	**Venclexta 100 mg tablets:** Override criteria were updated to approve the requested quantity, not to exceed 240 tablets per dispensing at retail or 720 tablets per dispensing at home delivery if the patient has systemic light chain amyloidosis or Waldenström macroglobulinemia/lymphoplasmacytic lymphoma.	04/19/2024