Venclexta® (venetoclax)
(Oral)

Document Number: IC-0276

Last Review Date: 05/04/2023
Date of Origin: 05/31/2016
Dates Reviewed: 05/2016, 04/2017, 04/2018, 12/2018, 05/2019, 06/2019, 05/2020, 05/2021, 05/2022, 05/2023

I. Length of Authorization [1,20]

Coverage will be provided for 6 months and may be renewed, unless otherwise specified.

- When used for CLL/SLL in combination with rituximab, coverage may be renewed up to a total 24 months of therapy (*from Day 1 of Cycle 1 of rituximab*).
- When used for CLL/SLL in combination with obinutuzumab, coverage may be renewed up until the end of 12 cycles of obinituzumab therapy (*Venetoclax therapy begins on Day 22 of Cycle 1 of obinituzumab*).
- When used for WM/LPL coverage may be renewed up to a total 24 months of therapy.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Venclexta Starting Pack: 1 pack per 28 days
- Venclexta 10 mg tablet: 2 tablets per day
- Venclexta 50 mg tablet: 1 tablet per day
- Venclexta 100 mg tablet: 12 tablets per day

B. Max Units (per dose and over time) [HCPCS Unit]:

- AML: 600 mg daily
- MCL, BPDCN, and WM/LPL: 800 mg daily
- MM and Amyloidosis: 1200 mg daily
- All other indications: 400 mg daily

III. Initial Approval Criteria [1]

Coverage is provided for treatment of the following conditions:

- Patient is at least 18 years of age, unless otherwise specified; **AND**

Universal Criteria [1]

- Patient must not receive live attenuated vaccines prior to, during, or after venetoclax treatment until B-cell recovery occurs; **AND**

- Patient will not receive concomitant therapy with moderate or strong CYP3A-inducers (e.g., rifampin, carbamazepine, phenytoin, St. John's Wort, etc.); **AND**

Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) † Φ [1,2,8-12]

- Patient will not receive concomitant therapy with strong CYP3A-inhibitors (e.g., ketoconazole, posaconazole, ritonavir, grapefruit products, Seville oranges, starfruit, etc.) during initiation and ramp-up phase; **AND**
    - Used in combination with obinutuzumab; **AND**
        - Used as first-line therapy; **OR**
        - Used as retreatment (if previously used as first-line therapy) for disease relapse after a period of remission in patients without del(17p)/TP53 mutation; **OR**
    - Used as a single agent or in combination with rituximab; **AND**
        - Patient has received at least one prior line of therapy

Acute Myeloid Leukemia (AML) † Φ [1-3,13,14]

- Used as induction therapy for newly diagnosed disease; **AND**
    - Used in combination with azacitidine, decitabine, or low-dose cytarabine; **AND**
        - Patient is a candidate for intensive therapy AND has poor-risk disease, therapy-related disease other than CBF-AML, antecedent MDS/CMML, or cytogenetic changes consistent with MDS (AML-MRC); **OR**
        - Patient is at least 75 years of age; **OR**
        - Patient is not a candidate for intensive induction therapy (e.g., PS ≥2, moderate hepatic impairment, severe cardiac or pulmonary disease, CL_{CR} < 45 mL/min, etc.); **OR**
- Used as post-induction therapy; **AND**
    - Used in combination with azacitidine, decitabine, or low-dose cytarabine; **AND**
    - Used following a response to previous lower intensity therapy with the same regimen; **OR**
- Used as consolidation therapy; **AND**
    - Used in combination with azacitidine, decitabine, or low-dose cytarabine; **AND**
    - Used as continuation of a low-intensity induction regimen; **AND**
        - Patient is <60 years of age; **OR**
        - Patient ≥60 years of age with poor-risk disease, therapy-related disease other than CBF-AML, antecedent MDS/CMML, or cytogenetic changes consistent with MDS (AML-MRC); **OR**
- Patient has relapsed/refractory disease; **AND**

- Used as a component of repeating the initial successful induction regimen in patients with late relapse (≥ 12 months since induction regimen) if not administered continuously and not stopped due to development of clinical resistance; **OR**
- Used in combination with azacitidine, decitabine, or low-dose cytarabine

Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) ‡ [2-5]

- Used in combination with azacitidine, decitabine, or low-dose cytarabine; **AND**
  - Patient has relapsed or refractory disease; **OR**
  - Patient has systemic disease with low performance status and/or nutritional status (i.e., serum albumin <3.2 g/dL) and is not a candidate for intensive remission therapy or tagraxofusp-erzs

Mantle Cell Lymphoma ‡ [2,6,7]

- Used as subsequent therapy; **AND**
  - Used as a single agent; **OR**
  - Used in combination with rituximab

Multiple Myeloma ‡ [2,15-17]

- Patient has relapsed or progressive disease with t(11;14) translocation; **AND**
- Used in combination with dexamethasone*****

*******Note: Treatment of patients with multiple myeloma with Venclexta in combination with bortezomib plus dexamethasone is not recommended outside of controlled clinical trials.*

Systemic Light Chain Amyloidosis ‡ [2,18,21]

- Patient has relapsed or refractory disease with t(11;14) translocation; **AND**
- Used as a single agent or in combination with dexamethasone

Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma (WM/LPL) ‡ [2,19,20]

- Used as single-agent therapy; **AND**
- Used as alternative therapy for previously treated disease; **AND**
  - Patient did not respond to primary therapy; **OR**
  - Patient has progressive or relapsed disease

† FDA Approved Indication(s); ‡ Compendia Approved Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,2,4-7,20]

Coverage can be renewed based on the following criteria:

- Patients continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: tumor lysis syndrome, severe neutropenia, severe infection, etc.; **AND**

Acute Myeloid Leukemia (AML)

- Disease stabilization or improvement as evidenced by a complete response [CR] (i.e., morphologic, cytogenetic or molecular complete response CR), complete hematologic response or a partial response by CBC, bone marrow cytogenic analysis, QPCR, or FISH

Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
    - Venetoclax/rituximab regimen: Patient has not received more than 24 months of therapy; **OR**
    - Venetoclax/obinutuzumab regimen: Patient has not received more than 12 cycles of therapy

Waldenström Macroglobulinemia / Lymphoplasmacytic Lymphoma (WM/LPL)

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Patient has not received more than 24 months of therapy

All other indications

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread

V. Dosage/Administration [1,3-7,15,16,20,21]

Indication	Dose
CLL/SLL	Dose titration schedule: • Week 1: 20 mg daily • Week 2: 50 mg daily • Week 3: 100 mg daily • Week 4: 200 mg daily • Week 5 and thereafter: 400 mg daily Monotherapy • 400 mg once daily after completing the 5-week dose ramp-up schedule. • Continue until disease progression or unacceptable toxicity. Rituximab combination therapy • Start rituximab administration after the patient has completed the 5-week dose ramp-up schedule with venetoclax and has received the 400 mg dose of venetoclax for 7 days. • Continue venetoclax 400 mg once daily for 24 months from Cycle 1 Day 1 of rituximab. Obinutuzumab combination therapy • On Cycle 1 Day 22, start venetoclax therapy according to the 5-week ramp-up schedule. After completing the ramp-up schedule on Cycle 2 Day 28, patients

Indication	Dose
	should continue Venclexta 400 mg once daily from Cycle 3 Day 1 until the last day of Cycle 12.
AML	Dose titration schedule: • Day 1: 100 mg daily • Day 2: 200 mg daily • Day 3: 400 mg daily • Days 4 and beyond: 400 mg daily (when used in combination with azacitidine or decitabine) or 600 mg daily (when used in combination with low-dose cytarabine) • Continue until disease progression or unacceptable toxicity
BPDCN	200 mg daily (NOTE: dosing can range from 100 mg to 800 mg daily)
Mantle Cell Lymphoma	Dose titration schedule: • Week 1: 20 mg daily • Week 2: 50 mg daily • Week 3: 100 mg daily • Week 4: 200 mg daily • Week 5 and thereafter: 400 mg daily • Dose may be escalated up to 800 mg daily at week 6 or later for patients with an insufficient response • Continue until disease progression or unacceptable toxicity
Multiple Myeloma/ Systemic Light Chain Amyloidosis	Dose titration schedule: • Week 1: 50-400 mg daily • Week 2 and thereafter: up to 1200 mg daily • Continue until disease progression or unacceptable toxicity
Waldenström Macroglobulinemia/ Lymphoplasmacytic Lymphoma	Dose-titrated from 200 mg to a maximum dose of 800 mg, daily for up to 2 years.

VI. Billing Code/Availability Information

HCPCS Code:

- J8999 – Prescription drug, oral, chemotherapeutic, Not Otherwise Specified

NDC:

- Venclexta Starting Pack: 00074-0579-xx
- Venclexta 10mg tablet: 00074-0561-xx
- Venclexta 50mg tablet: 00074-0566-xx
- Venclexta 100mg tablet: 00074-0576-xx

VII. References

1. Venclexta [package insert]. North Chicago, IL; Abbvie, Inc. June 2022. Accessed April 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) venetoclax. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C83.00	Small cell B-cell lymphoma, unspecified site
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C83.10	Mantle cell lymphoma, unspecified site
C83.11	Mantle cell lymphoma, lymph nodes of head, face, and neck
C83.12	Mantle cell lymphoma, intrathoracic lymph nodes
C83.13	Mantle cell lymphoma, intra-abdominal lymph nodes
C83.14	Mantle cell lymphoma, lymph nodes of axilla and upper limb
C83.15	Mantle cell lymphoma, lymph nodes of inguinal region and lower limb
C83.16	Mantle cell lymphoma, intrapelvic lymph nodes
C83.17	Mantle cell lymphoma, spleen
C83.18	Mantle cell lymphoma, lymph nodes of multiple sites
C83.19	Mantle cell lymphoma, extranodal and solid organ sites
C86.4	Blastic NK-cell lymphoma
C88.0	Waldenstrom macroglobulinemia
C90.00	Multiple myeloma not having achieved remission
C90.02	Multiple myeloma in relapse
C90.10	Plasma cell leukemia not having achieved remission
C90.12	Plasma cell leukemia in relapse
C90.20	Extramedullary plasmacytoma not having achieved remission
C90.22	Extramedullary plasmacytoma in relapse
C90.30	Solitary plasmacytoma not having achieved remission
C90.32	Solitary plasmacytoma in relapse
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse
C92.00	Acute myeloblastic leukemia not having achieved remission
C92.01	Acute myeloblastic leukemia, in remission
C92.02	Acute myeloblastic leukemia, in relapse
C92.50	Acute myelomonocytic leukemia not having achieved remission
C92.51	Acute myelomonocytic leukemia, in remission
C92.52	Acute myelomonocytic leukemia, in relapse
C92.60	Acute myeloid leukemia with 11q23-abnormality not having achieved remission

ICD-10	ICD-10 Description
C92.61	Acute myeloid leukemia with 11q23-abnormality in remission
C92.62	Acute myeloid leukemia with 11q23-abnormality in relapse
C92.A0	Acute myeloid leukemia with multilineage dysplasia not having achieved remission
C92.A1	Acute myeloid leukemia with multilineage dysplasia, in remission
C92.A2	Acute myeloid leukemia with multilineage dysplasia, in relapse
C93.00	Acute monoblastic/monocytic leukemia not having achieved remission
C93.01	Acute monoblastic/monocytic leukemia, in remission
C93.02	Acute monoblastic/monocytic leukemia, in relapse
E85.3	Secondary systemic amyloidosis
E85.4	Organ-limited amyloidosis
E85.81	Light chain (AL) amyloidosis
E85.89	Other amyloidosis
E85.9	Amyloidosis, unspecified
Z85.79	Personal history of other malignant neoplasms of lymphoid, hematopoietic and related tissues

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA,HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC