

Drug Policy:

Venclexta™ (venetoclax)

POLICY NUMBER UM ONC_1297	SUBJECT Venclexta™ (venetoclax)		DEPT/PROGRAM UM Dept	PAGE 1 of 3
DATES COMMITTEE REVIEWED 05/24/16, 06/29/17, 07/26/17, 07/19/18, 06/12/19, 12/11/19, 06/10/20, 05/12/21, 10/13/21, 11/15/21, 03/09/22, 05/11/22, 08/10/22, 11/09/22, 03/08/23, 05/10/23, 03/13/24	APPROVAL DATE March 13, 2024	EFFECTIVE DATE March 29, 2024	COMMITTEE APPROVAL DATES 05/24/16, 06/29/17, 07/26/17, 07/19/18, 06/12/19, 12/11/19, 06/10/20, 05/12/21, 10/13/21, 11/15/21, 03/09/22, 05/11/22, 08/10/22, 11/09/22, 03/08/23, 05/10/23, 03/13/24	
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT		
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Venclexta (venetoclax) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The requested medication was used within the last year, **AND**
2. The member has not experienced disease progression and/or no intolerance to the requested medication, **AND**
3. Additional medication(s) are not being added to the continuation request.

B. Acute Lymphoblastic Leukemia (ALL)

1. **NOTE:** Venclexta (venetoclax) + Chemotherapy (e.g., decitabine, hyper-CVAD, nelarabine, mini-hyper-CVD) is not supported by Evolent Policy for the treatment of relapsed/refractory ALL. This policy position is based on the lack of Level 1 Evidence (randomized clinical trials and/or meta-analyses) to show superior outcomes with Venclexta (venetoclax) +

Chemotherapy compared to Evolent recommended agents/regimens, including but not limited to regimens at <http://pathways.newcenturyhealth.com>.

C. Acute Myeloid Leukemia (AML)

1. Venclexta (venetoclax) may be used in combination with either Dacogen (decitabine), Vidaza (azacitidine), or low dose cytarabine for members with AML who have unfavorable-risk cytogenetics or are unsuitable for intensive remission induction therapy or decline intensive therapy; any of the above combinations may be used for remission induction therapy & post-remission therapy OR
2. Venclexta (venetoclax) may be used in combination with Dacogen (decitabine), Vidaza (azacitidine), or low dose cytarabine for members with relapsed/refractory AML

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

1. Venclexta (venetoclax) may be used in combination with Gazyva (obinutuzumab) as first or subsequent line therapy OR as a single agent with or without Gazyva (Obinutuzumab)/rituximab/rituximab biosimilar as subsequent line therapy for the treatment of CLL/SLL.

E. Mantle Cell Lymphoma

1. NOTE: [Venclexta (venetoclax) +/- rituximab] and [Venclexta (venetoclax) + Imbruvica (ibrutinib)] regimens are not supported by Evolent Policy based on the lack of Level 1 Evidence (randomized clinical trials and/or meta-analyses) to show superior outcomes with the above regimens compared to Evolent recommended agents/regimens, including but not limited to regimens at <http://pathways.newcenturyhealth.com>.

III. EXCLUSION CRITERIA

- A. Disease progression while taking Venclexta (venetoclax).
- B. Dosing exceeds single dose limit of Venclexta (venetoclax) 400 mg.
- C. Treatment exceeds the maximum limit of 120 (100 mg) or 120 (50 mg), 15 (10mg) tablets per month.
- D. Treatment exceeds the maximum months duration limit of 12 months (venetoclax only) when used in combination with Gazyva (obinutuzumab). Venclexta (venetoclax) + rituximab may be used up to 2 years duration limit.
- E. Investigational use of Venclexta (venetoclax) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
 1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
 2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
 3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
 4. Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it

- may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
 6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
 7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

- A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

- A. Review – Utilization Management Department
- B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

- A. None

VII. REFERENCES

- A. Jain N, et al. Ibrutinib and Venetoclax for First-Line Treatment of CLL. N Engl J Med. 2019 May 30;380(22):2095-2103.
- B. Fischer K, et al. Venetoclax and Obinutuzumab in Patients with CLL and Coexisting Conditions. N Engl J Med. 2019; 380 (23): 2225-2236. DOI: 10.1056/NEJMoa1815281
- C. DiNardo CD, et al. VIALE-A Clinical Trial. Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia. N Engl J Med. 2020 Aug 13;383(7):617-629.
- D. Seymour JF, et al. Venetoclax-Rituximab in Relapsed or Refractory Chronic Lymphocytic Leukemia. N Engl J Med. 2018 Mar 22;378(12):1107-1120.
- E. Venclexta prescribing information. Genentech USA, Inc. San Francisco, CA 2022.
- F. Clinical Pharmacology Elsevier Gold Standard 2023.
- G. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.
- H. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.
- I. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2023.
- J. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. 2014 Apr 20;32(12):1277-80.
- K. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>.