Evolent Clinical Guideline 3051 for Venclexta™ (venetoclax)

Guideline Number:	Applicable Codes	
Evolent_CG_3051		
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc.		
Original Date:	**Last Revised Date:**	**Implementation Date:**
May 2016	March 2025	March 2025

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STATEMENT

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.

INDICATIONS

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

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Acute Lymphoblastic Leukemia (ALL)

- 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 **Evolent Pathways**.

Acute Myeloid Leukemia (AML)

- 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
- Venclexta (venetoclax) may be used in combination with Dacogen (decitabine), Vidaza (azacitidine), or low dose cytarabine for members with relapsed/refractory AML

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

- 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.

Mantle Cell Lymphoma

- 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 **Evolent Pathways**

CONTRAINDICATIONS/WARNINGS

- None

EXCLUSION CRITERIA

- Disease progression while taking Venclexta (venetoclax).
- Dosing exceeds single dose limit of Venclexta (venetoclax) 400 mg.
- Treatment exceeds the maximum limit of 120 (100 mg) or 120 (50 mg), 15 (10mg) tablets per month.
- 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.
- 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:
    - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
    - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
    - 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.
    - 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).
    - 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.

- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- 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.

CODING AND STANDARDS

Codes

- J8999 - venetoclax

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
March 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1297 Venclexta (venetoclax)
March 2024	• Updated references • Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

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2. Lunsumio prescribing information. Genentech, Inc. South San Francisco, CA 2024.
3. Clinical Pharmacology Elsevier Gold Standard 2025.
4. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
5. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
6. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
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8. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.
9. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.