Clinical Policy: Venetoclax (Venclexta)

Reference Number: PA.CP.PHAR.129
Effective Date: 10.17.18
Last Review Date: 04/2019 Revision Log

Description
Venetoclax (Venclexta®) is a B-cell lymphoma 2 protein (BCL-2) inhibitor.

FDA Approved Indication(s)
Venclexta is indicated:

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

**This indication is approved under accelerated approval based on response rates. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.*

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness® that Venclexta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma (must meet all)**:**

1. Diagnosis of CLL or SLL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Request meets one of the following (a or b):
   a. Dose does not exceed 400 mg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

B. Mantle Cell Lymphoma (off-label) (must meet all)**:**

1. Diagnosis of mantle cell lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Member has received appropriate prior therapy [induction therapy or chemoimmunotherapy (e.g., RDHAP: Rituxan, dexamethasone, cytarabine, cisplatin; RDHAX: Rituxan, dexamethasone, cytarabine, oxaliplatin; bendamustine plus Rituxan; VR-CAP: bortezomib, Rituxan, cyclophosphamide, doxorubicin, and prednisone)];
4. Request meets one of the following (a or b):
   a. Dose does not exceed 400 mg per day;

b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

C. Acute Myeloid Leukemia (must meet all)**:**

1. Diagnosis of AML;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Member meets one of the following (a or b):
   a. Age ≥ 60 years;
   b. Medical justification supports inability to use intensive induction chemotherapy (see *Appendix D* for examples);
4. Prescribed in combination with azacitidine, decitabine, or low-dose (20 mg/m^2) cytarabine;
5. Request meets one of the following (a, b, or c):
   a. In combination with azacitidine or decitabine: Dose does not exceed 400 mg per day;
   b. In combination with low-dose cytarabine: Dose does not exceed 600 mg per day;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

D. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. For AML, prescribed in combination with azacitidine, decitabine, or low-dose (20 mg/m^2) cytarabine;
4. If request is for a dose increase, request meets one of the following (a, b, or c):
   a. CLL, SLL, or in combination with azacitidine or decitabine for AML: New dose does not exceed 400 mg per day;
   b. In combination with low-dose cytarabine for AML: New dose does not exceed 600 mg per day;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care Policy (PA.LTSS.PHAR.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AML: acute myeloid leukemia
BCL-2: B-cell lymphoma 2 protein
CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
SLL: small lymphocytic lymphoma

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Imbruvica® (ibrutinib)	Three 140 mg capsules (420 mg) PO QD	420 mg/day
Arzerra® (ofatumumab)	Varies	Varies
fludarabine (Fludara®, Oforta®), cyclophosphamide (Cytoxan®, Neosar®) and Rituxan® (rituximab) (FCR)	Varies	Varies
fludarabine plus Rituxan® (rituximab) (FR)	Varies	Varies
Leukeran® (chlorambucil)	Varies	Varies
bendamustine (Treanda®, Bekenda®) plus Rituxan® (rituximab)	Varies	Varies
pentostatin (Nipent®), cyclophosphamide and Rituxan® (rituximab) (PCR)	Varies	Varies
high-dose methylprednisolone with Rituxan® (rituximab)	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): concomitant use of Venclexta with strong inhibitors of CYP3A at initiation and during ramp-up phase in patients with CLL/SLL
- Boxed warning(s): none reported

Appendix D: General Information

- The management of AML is divided into induction and postremission (consolidation) therapy. Induction usually includes intensive chemotherapy (e.g., standard [100-200

mg/m^2] or high [2 g/m^2] dose cytarabine, fludarabine), but many adults with AML are unable to undergo intensive chemotherapy due to its toxicities. Some examples of reasons why members may not qualify for intensive induction chemotherapy include, but are not limited to:
  - Baseline Eastern Cooperative Oncology Group (ECOG) performance status of 2-3
  - Severe cardiac comorbidity (e.g., history of congestive heart failure requiring treatment, ejection fraction ≤ 50%, or chronic stable angina)
  - Severe pulmonary comorbidity (e.g., carbon monoxide diffusing capacity [DLCO] ≤ 65% or forced expiratory volume in one second [FEV_1] ≤ 65%)
  - Moderate hepatic impairment
  - Creatinine clearance < 45 mL/min or baseline creatinine > 1.3 mg/dL
- For AML, the NCCN recommends the use of Venclexta in patients ≥ 60 years of age who are (category 2A for both):
  - Not candidates for intensive induction chemotherapy
  - Candidates for intensive induction chemotherapy, and have unfavorable cytogenetic/molecular markers/antecedent hematologic disorder/therapy-related AML

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CLL and SLL	<u>Venclexta 5-week dose ramp-up schedule:</u> 20 mg PO QD for one week followed by 50 mg PO QD for one week, 100 mg PO QD for one week, 200 mg PO QD for one week, then 400 mg PO QD <u>Venclexta in combination with rituximab:</u> Administer rituximab after the 5-week ramp-up schedule with Venclexta. Continue Venclexta 400 mg QD for 24 months from Cycle 1 Day 1 of rituximab. <u>Venclexta as monotherapy:</u> 400 mg PO QD after the patient has completed the 5-week dose ramp-up schedule until disease progression or unacceptable toxicity	400 mg/day

AML	PO QD in combination with azacitidine, decitabine, or low-dose cytarabine:
	• Day 1: 100 mg/day
	• Day 2: 200 mg/day
	• Day 3: 400 mg/day
	• Day 4 and beyond, until disease progression or unacceptable toxicity:
	  o In combination with azacitidine or decitabine: 400 mg/day
	  o In combination with low-dose cytarabine: 600 mg/day
		400 mg/day with azacitidine or decitabine; 600 mg/day with cytarabine

VI. Product Availability

Tablets: 10 mg, 50 mg, 100 mg

VII. References

1. Venclexta Prescribing Information. North Chicago, IL: AbbVie Inc.; May 2019. Available at: https://www.venclexta.com. Accessed June 6, 2019.
2. Seymour JF, Kipps TJ, Eichhorst B, et al. Venetoclax-rituximab in relapsed or refractory chronic lymphocytic leukemia, N Engl J Med 2018; 378: 1107-1120.
3. Stilgenbauer S, Eichhorst B, Schetelig J, et al. Venetoclax in relapsed or refractory chronic lymphocytic leukaemia with 17p deletion: a multicentre, open-label, phase 2 study. The Lancet Oncology 2016;17(6):768-778.
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5. Coutre S, Choi M, Furman RR, et al. Venetoclax for patients with chronic lymphocytic leukemia who progressed during or after idelalisib therapy. Blood 2018; 131(15): 1704-1711.
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7. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed June 6, 2019.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created:	10/18	
Criteria added for new FDA indication: AML; references reviewed and updated.	04/19	