venetoclax (Venclexta®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO071

Description

Venetoclax (Venclexta) is an orally administered B-cell lymphoma-2 (BCL-2) inhibitor.

Length of Authorization

- Initial:
  - i. Previously untreated CLL/SLL: 12 months
  - ii. All other indications: Six months
- Renewal:
  - i. Previously untreated CLL/SLL: Cannot be renewed
  - ii. All other indications: 12 months

Quantity limits

Product Name	Dosage Form	Indication	Quantity Limit	DDID
venetoclax (Venclexta)	Starter Pack	Chronic lymphocytic leukemia (CLL); Small lymphocytic lymphoma (SLL)	1 pack/28 days	192575
	10 mg tablets		28 tablets/28 days	192576
	50 mg tablets		28 tablets/28 days	192577
	100 mg tablets		120 tablets/30 days	192579
	100 mg tablets	Acute myeloid leukemia	180 tablets/30 days	192579

Initial Evaluation

I. Venetoclax (Venclexta) may be considered medically necessary when the following criteria below are met:
   A. Prescribed by or in consultation with an oncologist or hematologist; **AND**
   B. A diagnosis of:
      1. **Relapsed/refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)**; **AND**
         i. Received at least one prior therapy [e.g., Imbruvica (ibrutinib) or chemotherapy-containing regimen]; **AND**

ii. Will be used as monotherapy or in combination with rituximab (Rituxan); **OR**

2. **Previously untreated chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL); AND**
   i. Will be used in combination with obinutuzumab (Gazyva); **OR**
3. **Newly-diagnosed acute myeloid leukemia (AML)**; **AND**
   i. Age 75 years and older; **OR**
   ii. Have comorbidities that preclude use of intensive induction chemotherapy such as:
      a. Baseline Eastern Cooperative Oncology Group (ECOG) performance status of 2-3
      b. Severe cardiac or pulmonary comorbidity
      c. Moderate hepatic impairment
      d. CrCL ≥30 to <45 mL/min

   AND
   iii. Used in combination with azacitidine or decitabine or low-dose cytarabine

II. Venetoclax (Venclexta) is considered investigational for all other conditions, including but not limited to:
   A. Acute Myeloid Leukemia – Previously treated
   B. Multiple Myeloma (MM)
   C. Previously untreated CLL/SLL – Treatment for more than 12 months

Renewal Evaluation

I. Member has a diagnosis of relapsed/refractory CLL/SLL or newly diagnosed AML; **AND**
II. Clinical documentation of response to treatment, such as stabilization or improvement of disease; **AND**
III. Absence of unacceptable toxicity from the medication

Supporting Evidence

I. Venetoclax (Venclexta) is FDA-approved for the treatment of CLL/SLL, in adult patients with or without 17p deletion.
II. Patients included in venetoclax (Venclexta) monotherapy studies in CLL/SLL were relapsed/refractory to fludarabine-based regimens (e.g. Rituximab+Fludarabine+Cyclophosphamide, Fludarabine+Rituximab, Fludarabine+Cyclophosphamide) or alkylator- based regimens (e.g. chlorambucil, bendamustine), or to ibrutinib (Imbruvica)or idelasilib (Zydelig). Patients included in the

venetoclax (Venclexta) plus rituximab (Rituxan) trial (MURANO) for relapsed CLL/SLL had received one to three previous treatments (including at least one chemotherapy-containing regimen). Prior radiation therapy or stem cell transplant alone is not considered a prior therapy as this treatment strategy alone was not considered an inclusion in pivotal trials.

III. Venetoclax (Venclexta) approval in untreated CLL/SLL was based on the findings from the CLL14 randomized, open label, phase 3 trial. CLL14 evaluated the safety and efficacy of fixed-duration treatment with venetoclax (Venclexta) in combination with obinutuzumab (VEN+G) versus obinutuzumab in combination with chlorambucil (GClb) for patients with previously untreated CLL with coexisting medical conditions. Patients received 12 months of venetoclax (Venclexta) in combination with six cycles of obinutuzumab. The trial met its primary outcome of progression-free survival (PFS) in patients treated with Venclexta plus obinutuzumab compared to patients who received chlorambucil plus obinutuzumab, a commonly used standard of care. After a median follow-up of 28 months, Venclexta plus obinutuzumab reduced the risk of progression or death by 67% compared with chlorambucil plus obinutuzumab (hazard ratio: 0.33, 95% confidence interval [CI]: 0.22, 0.51; p<0.0001).
The majority of patients receiving Venclexta in the trial remained progression-free at two years.

IV. FDA granted accelerated approval to venetoclax (Venclexta) for use in combination with azacitidine or decitabine or low-dose cytarabine for the treatment of adult patients with newly-diagnosed acute myeloid leukemia (AML) who are aged 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy. Approval is based on 2 phase Ib/II trials in this setting. Continued approval of venetoclax (Venclexta) in AML is contingent on the results of a confirmatory trial.

Investigational or Not Medically Necessary Uses

I. Acute Myeloid Leukemia – Previously treated
   A. Pivotal trials leading to FDA approval were specifically in the previously untreated setting. Use in the relapsed/refractory setting is not supported by clinical trials nor cited within NCCN AML guidelines.

II. Multiple Myeloma (MM)
   A. Venetoclax (Venclexta) is currently being evaluated for use in MM and is the subject of ongoing clinical trials. As of March 2019, “FDA reviewed data from the BELLINI clinical trial (NCT02755597, Study M14-031) evaluating the use of Venetoclax (Venclexta) combined with bortezomib and dexamethasone in patients with multiple myeloma. The interim trial results demonstrated an increased risk of death for patients receiving Venetoclax (Venclexta) as compared to the control group. On March 6, 2019, the FDA required no new patients be enrolled on the Bellini trial. The FDA suspended enrollment in other ongoing multiple myeloma clinical trials of Venclexta.”

III. Previously untreated CLL/SLL – Treatment for more than 12 months

A. Venetoclax (Venclexta) approval in untreated CLL/SLL was based on the findings from the CLL14 randomized, open label, phase 3 trial. CLL14 evaluated the safety and efficacy of fixed-duration treatment with venetoclax (Venclexta) in combination with obinutuzumab (VEN+G) versus obinutuzumab in combination with chlorambucil (GClb). Patients received 12 months of venetoclax (Venclexta) in combination with six cycles of obinutuzumab. Treatment beyond 12 months has not been evaluated.

References

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Policy Implementation/Update:

venetoclax (Venclexta®)

EOCCO POLICY

Date Created	June 2016
Date Effective	August 2016
Last Updated	June 2019
Last Reviewed	06/2016, 08/2018, 12/2018, 06/2019

Action and Summary of Changes	**Date**
Added new FDA approval in untreated CLL/SLL in combination with obinutuzumab (Gazyva)	06/2019
Added new FDA approval in Acute Myeloid Leukemia.	12/2018
Included new FDA expanded indication in CLL/SLL without 19p deletion and expanded initial approval to 6 months.	08/2018