PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Venclexta® (venetoclax tablets – AbbVie and Genentech)

TAC APPROVAL DATE: 06/05/2019

OVERVIEW
Venclexta, a B-cell lymphoma-2 (BCL-2) inhibitor, is indicated for the treatment of adults with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). Additionally, Venclexta is indicated for use in combination with azacitidine or decitabine or low-dose cytarabine for the treatment of newly-diagnosed acute myeloid leukemia in adults who are ≥ 75 years of age 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.

Guidelines
The National Comprehensive Cancer Network (NCCN) guidelines for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (SLL) [version 5.2019 – May 23, 2019] cite Venclexta in several scenarios. Venclexta plus Gazyva® (obinutuzumab injection for intravenous use) is listed as a first-line therapy (preferred regimen) in frail patients with comorbidities without 17p deletion/TP53 mutation (Category 2A). This regimen is also cited as another recommended regimen (Category 2B) in patients < 65 years of age without significant comorbidity. Venclexta plus rituximab is listed as preferred regimen option for patients with relapsed/refractory therapy without 17p deletion (Category 1). The NCCN also cite Venclexta as an option for relapsed/refractory therapy among patients with CLL without deletion 17p/TP53 mutation (Category 2A). For patients with 17p deletion/TP53 mutation, Venclexta plus Gazyva is recommended as a preferred regimen (Category 2A). Also, among this population, Venclexta with rituximab (Category 1) and Venclexta alone (Category 2A) are recommended in patients with relapsed or refractory disease. Many other first-line options are recommended. CLL and SLL are different manifestations of the same diseases which are managed similarly.

NCCN guidelines for AML (version 3.2019 – May 7, 2019) recommend Venclexta (in combination with decitabine, azacitidine or low-dose cytarabine) for treatment induction in patients ≥ 60 years of age who are candidates for intensive remission induction therapy with unfavorable-risk cytogenetics. Venclexta (along with decitabine, azacitidine, or low-dose cytarabine) is also recommended as AML post-remission therapy for patients ≥ 60 years of age.

The NCCN guidelines for B-Cell Lymphomas (version 3.2019 – May 6, 2019) address mantle cell lymphoma. Venclexta is sited as a preferred second-line therapy regimen (Category 2A). Other regimens recommended second-line are Venclexta plus Imbruvica (Category 2B).

POLICY STATEMENT
Prior authorization is recommended for prescription benefit coverage of Venclexta.

Automation: None.
RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Venclexta is recommended in those who meet the following criteria:

FDA-Approved Indications

1. Chronic Lymphocytic Leukemia (CLL). Approve for 3 years.

2. Small Lymphocytic Lymphoma (SLL). Approve for 3 years.

3. Acute Myeloid Leukemia (AML). Approve for 3 years if the patient is using Venclexta in combination with either azacitidine, decitabine, or cytarabine.

Other Uses with Supportive Evidence

4. Mantle Cell Lymphoma. Approve for 3 years if the patient has tried one prior therapy (e.g., Imbruvica® [ibrutinib capsules and tablets] with or without rituximab; Calquence® [acalabrutinib capsules]; Revlimid® [lenalidomide capsules] with or without rituximab; RDHAP (rituximab, dexamethasone, cytarabine, cisplatin); RDHAX [rituximab, dexamethasone, cytarabine, oxaliplatin]; alternating RCHOP/RDHAP [rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone/rituximab, dexamethasone, cytarabine, cisplatin]; HyperCVAD [cyclophosphamide vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine] plus rituximab; RCHOP; or Treanda® [bendamustine injection for intravenous use] plus rituximab).

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Venclexta has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES
1. Venclexta® tablets [prescribing information]. North Chicago, IL and South San Francisco, CA: AbbVie and Genentech (a member of the Roche Group); May 2019.
## HISTORY

<table>
<thead>
<tr>
<th>Type of Revision</th>
<th>Summary of Changes</th>
<th>TAC Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual revision</td>
<td>Added criteria for mantle cell lymphoma and small lymphocytic lymphoma per NCCN guidelines. The alternatives were changed for patients with CLL and CLL with 17p deletion in-line with NCCN guidelines.</td>
<td>05/16/2018</td>
</tr>
<tr>
<td>Annual revision</td>
<td>Criteria were updated to reflect that Venclexta is now FDA-approved for CLL with or without the 17p deletion. Prior to this, the product was FDA-approved only for 17p deletion CLL; however, the criteria previously addressed both settings. The specific approval condition and related criteria for CLL with 17p deletion were deleted. The criteria for CLL was moved from the Other Uses with Supportive Evidence Section to the FDA-Approved Indications section. The alternatives cited that qualify as a trial of one prior therapy for CLL, which is required before approval, were merged such that no changes were needed in the listing of agents. Criteria were updated to reflect that Venclexta is now indicated for SLL, with or without 17p deletion. The criteria addressing SLL, which require that the patient has tried one prior therapy, was moved from the Other Uses with Supportive Evidence Section to the FDA-approved indications section.</td>
<td>06/20/2018</td>
</tr>
<tr>
<td>Selected revision</td>
<td>Criteria were updated to reflect that Venclexta is now FDA-approved for CLL with or without the 17p deletion. Prior to this, the product was FDA-approved only for 17p deletion CLL; however, the criteria previously addressed both settings. The specific approval condition and related criteria for CLL with 17p deletion were deleted. The criteria for CLL was moved from the Other Uses with Supportive Evidence Section to the FDA-Approved Indications section. The alternatives cited that qualify as a trial of one prior therapy for CLL, which is required before approval, were merged such that no changes were needed in the listing of agents. Criteria were updated to reflect that Venclexta is now indicated for SLL, with or without 17p deletion. The criteria addressing SLL, which require that the patient has tried one prior therapy, was moved from the Other Uses with Supportive Evidence Section to the FDA-approved indications section.</td>
<td>06/20/2018</td>
</tr>
<tr>
<td>Selected revision</td>
<td>Criteria added to address the new indication for AML.</td>
<td>11/28/2018</td>
</tr>
<tr>
<td>Annual revision</td>
<td>Criteria regarding the diagnosis of AML were revised per guidance from updated NCCN guideline for AML (version 1.2019 – January 18, 2019). The following criteria were removed regarding this diagnosis: 1) the patient is ≥ 75 years of age, and 2) according to the prescribing physician, the patient has comorbidities that preclude the use of intensive induction chemotherapy.</td>
<td>02/06/2018</td>
</tr>
<tr>
<td></td>
<td>1. Chronic Lymphocytic Leukemia: The requirement of a trial of one prior therapy prior to approval was removed. 2. Small Lymphocytic Lymphoma: The requirement of a trial of one prior therapy prior to approval was removed. 3. Mantle Cell Lymphoma: For clarity, in criteria, the reference to Rituxan when listing previous required therapies was changed to “rituximab”.</td>
<td>06/05/2019</td>
</tr>
</tbody>
</table>

† For a further summary of criteria changes, refer to respective TAC minutes available at: [http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx](http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx); TAC – Therapeutic Assessment Committee; CLL – Chronic lymphocytic leukemia; FCR – Fludarabine, cyclophosphamide and Rituxan; FR – Fludarabine and Rituxan; NCCN – National Comprehensive Cancer Network; SLL – Small lymphocytic leukemia; AML – Acute myeloid leukemia.