PRIOR AUTHORIZATION POLICY

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

DATE REVIEWED: 06/03/2020

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).[1] 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 (AML) 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.

Disease Overview

CLL is one of the most prevalent adult leukemias in the Western world.[2] In 2019, an estimated 20,720 patients will be diagnosed with CLL in the US, and approximately 3,930 patients will die from the disease. The condition usually is diagnosed in older adults (≥ 70 years of age) and occurs more frequently in men. The leukemic cells appear as small, mature lymphocytes. CLL and SLL are different manifestations of the same condition and are managed similarly. In CLL, many of the abnormal lymphocytes are found in the blood, as well as in the bone marrow and lymphoid tissue. In SLL, there are few, if any, abnormal lymphocytes circulating in blood and most of the disease is in the lymph nodes, bone marrow, and other lymphoid tissue. The diagnosis requires the presence of at least 5 x 10^9/L monoclonal B-lymphocytes in the peripheral blood. SLL requires the presence of lymphadenopathy and/or splenomegaly with < 5 x 10^9/L B-lymphocytes found in the peripheral blood.

AML is a heterogeneous hematologic malignancy that is hallmarked by clonal expansion of myeloid blasts in the peripheral blood, bone marrow, and/or other tissues.[3] It is a rather common form of acute leukemia in adults and it has the largest number of annual deaths from leukemias in the US. Around 21,450 people will be diagnosed with AML in 2019, and 10,920 patients will die from the condition. The median age at diagnosis is 67 years. Over one-half and approximately one-third of patients receive the diagnosis at ≥ 65 and ≥ 75 years of age, respectively. The incidence of AML, along with myelodysplastic syndrome (MDS) is rising as patients become older. Environmental factors play a role and include prolonged exposure to petrochemicals; solvents such as benzene; pesticides; and ionizing radiation. Also, two cytotoxic agents that are associated with therapy-related MDS/AML are alkylating agents (e.g., cyclophosphamide) and topoisomerase inhibitors (e.g., doxorubicin). Antimetabolite therapy, notably fludarabine, has also been associated with MDS/AML in patients with lymphoproliferative disorders, especially when given in combination with alkylating agents. Molecular or karyotypic abnormalities can also be identified. Treatment of AML can involve the following modalities at various stages: chemotherapy, radiation therapy, chemotherapy with stem cell transplant, and other drug therapy.

Guidelines

The National Comprehensive Cancer Network (NCCN) guidelines for CLL/SLL (version 4.2020 – December 20, 2019) cite Venclexta in several scenarios.[2] Venclexta plus Gazyva® (obinutuzumab injection for intravenous use) is listed as a first-line therapy (preferred regimen) in frail patients with comorbidities, patients ≥ 65 years, and in younger patients with significant 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).[3] The NCCN also cite Venclexta as an option for relapsed/refractory therapy among patients with CLL without deletion 17p/TP53 mutation (category 2A).[3] For patients with 17p deletion/TP53 mutation, Venclexta plus Gazyva is recommended as a preferred regimen first-line (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 as preferred regimens. Many other first-line options are recommended. CLL and SLL are different manifestations of the same diseases which are managed similarly.[3]

NCCN guidelines for AML (version 3.2020 – December 23, 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.[3] It is also recommended in other induction therapy clinical scenarios in patients who are not candidates for intensive remission. . Venclexta (along with decitabine, azacitidine, or low-dose cytarabine) is also recommended as AML post-induction therapy for patients ≥ 60 years of age.

The NCCN guidelines for B-Cell Lymphomas (version 1.2020 – January 22, 2020) address mantle cell lymphoma. Venclexta is cited as a preferred second-line therapy regimen (category 2A) in patients with a short response duration to prior chemoimmunotherapy.[4] Other regimens recommended second-line are Venclexta plus Imbruvica (category 2B). Venclexta is recommended as an other recommended regimen in patients with an extended response duration to prior chemoimmunotherapy.

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 at least one prior therapy. Note: Examples of therapies include Imbruvica® (ibrutinib capsules and tablets) with or without rituximab; Calquence® (acalabrutinib capsules); Revlimid® (lenalidomide capsules) with or without rituximab; RDHAP (rituximab, dexamethasone, cytarabine, cisplatin); 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); July 2019.
2. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (Version 4.2020 – December 20, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at http://www.nccn.org. Accessed on May 28, 2020.
3. The NCCN Acute Myeloid Leukemia Clinical Practice Guidelines in Oncology (Version 3.2020 – December 23, 2019). © 2019 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on May 28, 2020.
4. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (Version 1.2020 – January 22, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at http://www.nccn.org. Accessed on May 28, 2020.