PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Venclexta Prior Authorization Policy
- Venclexta® (venetoclax tablets – AbbVie and Genentech)

REVIEW DATE: 06/12/2024; selected revision 12/18/2024

OVERVIEW

Venclexta, a B-cell lymphoma-2 inhibitor, is indicated in adults for the following uses:[1]

- **Acute myeloid leukemia (AML)**, in combination with azacitidine or decitabine or low-dose cytarabine for newly diagnosed AML in patients ≥ 75 years of age or who have comorbidities that preclude use of intensive induction chemotherapy.
- **Chronic lymphocytic leukemia (CLL)**.
- **Small lymphocytic lymphoma (SLL)**.

Guidelines

Venclexta is discussed in guidelines from the National Comprehensive Cancer Network (NCCN):

- **Acute Lymphoblastic Leukemia (ALL)**: NCCN pediatric ALL guidelines (version 5.2024 – April 3, 2024) recommend a Venclexta-containing regimen (i.e. Venclexta, vincristine, Oncaspar® [pegaspargase intravenous infusion or intramuscular injection] or Asparlas® [calaspargase pegol-mknl intravenous infusion], and prednisone or dexamethasone) for relapsed or refractory ALL as "other recommended regimens" (category 2A).[2] NCCN adult and adolescent ALL guidelines (version 4.2023 – February 5, 2024) recommend Venclexta + chemotherapy for relapsed or refractory ALL as "other recommended regimens" (category 2B).[3]
- **AML**: NCCN guidelines (version 3.2024 – May 17, 2024) recommend Venclexta (in combination with decitabine, azacitidine or low-dose cytarabine) in a variety of clinical scenarios, such as induction therapy, post induction therapy, and relapsed or refractory disease.[4] The guidelines recommend Venclexta (in combination with decitabine, azacitidine, or low-dose cytarabine) for Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) for systemic disease treated with palliative intent (patients with low performance and/or nutritional status) or relapsed/refractory disease (category 2A).[4]
- **B-Cell Lymphomas**: NCCN guidelines (version 2.2024 – April 30, 2024) address mantle cell lymphoma.[5] The guidelines cite Venclexta (continuous) ± rituximab and Venclexta + Imbruvica® (ibrutinib tablets, capsules, and oral solution) as second-line therapy and subsequent therapy as "useful in certain circumstances" (both category 2A).[5] Venclexta in combination with Brukinsa (zanubrutinib capsules) and Gazyva® (obinutuzumab intravenous infusion) is also recommended as induction therapy for mantle cell lymphoma with a classical or indolent *TP53* mutation (category 2A) in absence of a clinical trial.[5]
- **CLL/SLL**: NCCN guidelines (version 3.2024 – March 26, 2024) cite Venclexta in several scenarios.[6] For patients without 17p deletion/TP53 mutation, Venclexta + Gazyva is listed as a "preferred" first-line therapy (category 1); Venclexta + rituximab is listed as a "preferred regimen" (category 1), single-agent Venclexta is listed as "other recommended regimen" (category 2A), and Venclexta ± anti-CD20 monoclonal antibody (Venclexta + Gazyva preferred) is listed as "useful in certain circumstances" (category 2A) for second-line or third-line therapy.[6] For patients with 17p deletion/TP53 mutation, Venclexta + Gazyva is recommended as a "preferred regimen" first-line therapy (category 2A); Venclexta + rituximab (category 1), single-agent Venclexta (category 2A) are "preferred" and Venclexta ± anti-CD20 monoclonal antibody (Venclexta + Gazyva preferred) is listed as "useful in certain circumstances" (category 2A) for second-line and

subsequent therapy in this population. Venclexta is also recommended other clinical scenarios as well. Many other first-line options are recommended. CLL and SLL are different manifestations of the same disease which are managed similarly.

- **Hairy Cell Leukemia**: NCCN guidelines (version 2.2024 – April 22, 2024) recommend Venclexta ± rituximab for progressive disease after relapsed/refractory therapy in patients with disease resistant to *BRAF* inhibitor therapy as "useful in certain circumstances" (category 2A).[7]
- **Myelodysplastic Syndromes:** NCCN guidelines (version 1.2025 – November 15, 2024) recommend Venclexta for the management of higher-risk disease (i.e. International prognostic scoring system [IPSS-R] intermediate-, high-, or very-high risk disease) in combination with a hypomethylating agent (azacitidine or decitabine) and for the treatment of chronic myelomonocytic leukemia (CMML)-2 in combination with a hypomethylating agent (azacitidine or decitabine) [category 2A].[8]
- **Myeloproliferative Neoplasms**: NCCN guidelines (version 1.2024 – December 21, 2023) recommend Venclexta + hypomethylating agents (e.g. azacitidine or decitabine) for accelerated or blast phase myeloproliferative neoplasms as management of disease progression (category 2A).[9]
- **Multiple Myeloma:** NCCN guidelines (version 4.2024 – April 26, 2024) recommend Venclexta + dexamethasone ± Darzalex® (daratumumab intravenous infusion) for previously treated multiple myeloma for relapse or refractory disease for patients with t (11;14) translocation as "useful in certain circumstances" after 1-3 prior therapies) [category 2A].[10]
- **Systemic Light Chain Amyloidosis:** NCCN guidelines (version 2.2024 – December 12, 2023) list Venclexta ± dexamethasone as a therapy for previously treated disease for patients with t (11;14) translocation as "useful in certain circumstances" (category 2A).[11]
- **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma:** NCCN guidelines (version 2.2024 – December 5, 2023) recommend single-agent Venclexta as "other recommended regimen" for previously treated disease (category 2A).[12]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Venclexta. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Venclexta is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Acute Myeloid Leukemia.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   Note: Acute Myeloid Leukemia includes Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN).
   A) Patient is ≥ 18 years of age; AND
   B) Venclexta is used in combination with either azacitidine, decitabine, or cytarabine.

2. **Chronic Lymphocytic Leukemia.** Approve for 1 year if the patient is ≥ 18 years of age.

3. **Small Lymphocytic Lymphoma.** Approve for 1 year if the patient is ≥ 18 years of age.

Other Uses with Supportive Evidence

4. **Acute Lymphoblastic Leukemia.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient has relapsed or refractory disease; AND
   B) This medication will be used in combination with chemotherapy.

5. **Hairy Cell Leukemia.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has disease resistance to *BRAF* inhibitor therapy.
   Note: Examples of *BRAF* inhibitor therapy include Tafinlar (dabrafenib capsules and oral tablets for suspension) and Zelboraf (vemurafenib tablets).

6. **Mantle Cell Lymphoma.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following (i or ii):
      i. Patient has tried at least one systemic regimen; OR
      Note: Examples of systemic regimens include those containing one or more of the following products: Imbruvica (ibrutinib tablets, capsules, and oral solution), rituximab, Calquence (acalabrutinib tablets), lenalidomide, dexamethasone, cytarabine, cisplatin, cyclophosphamide, doxorubicin, vincristine, high-dose methotrexate, cytarabine, or Treanda (bendamustine intravenous infusion).
      ii. Patient meets BOTH of the following (a and b):
         a) Patient has a *TP53* mutation; AND
         b) The medication is used as induction therapy in combination with Brukinsa (zanubrutinib capsules) and Gazyva (obinutuzumab intravenous infusion).

7. **Myelodysplastic Syndrome**. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient meets ONE of the following (i or ii):
      i. Patient has chronic myelomonocytic leukemia-2; OR
      ii. Patient has higher risk disease; AND
      Note: Higher risk disease includes patients who have an international prognostic scoring system (IPSS-R) intermediate-, high-, or very-high risk disease.
   C) The medication is used in combination with azacitidine or decitabine.

8. **Myeloproliferative Neoplasm**. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has accelerated or blast phase disease; AND
   C) The medication is used in combination with azacitidine or decitabine.

9. **Multiple Myeloma**. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 18 years of age; AND
   B) Patient has t (11;14) translocation; AND
   C) Patient has tried at least one systemic regimen for multiple myeloma; AND
   Note: Examples of systemic regimens include those containing one or more of the following products: bortezomib, Kyprolis (carfilzomib intravenous injection), lenalidomide, cyclophosphamide, or Ninlaro (ixazomib capsules).
   D) Venclexta is used in combination with dexamethasone.

10. Systemic Light Chain Amyloidosis. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has t (11;14) translocation; AND
- **C)** Patient has tried at least one systemic regimen.
  Note: Examples of systemic regimens include those containing one or more of the following products: bortezomib, lenalidomide, cyclophosphamide, and melphalan.

11. Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma. Approve for 1 year if the patient meets ALL of the following (A and B):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has tried at least one systemic regimen.
  Note: Examples of a systemic regimen contain one or more of the following products: Brukinsa (zanubrutinib capsules), Imbruvica (ibrutinib tablets, capsules, and oral solution), rituximab, bendamustine, cyclophosphamide, dexamethasone, bortezomib, fludarabine, or cladribine.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Venclexta is not recommended in the following situations:

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; June 2022.
2. The NCCN Pediatric Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 5.2024 – April 3, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 10, 2024.
3. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 4.2023 – February 5, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 10, 2024.
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5. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 2.2024 – April 30, 2024). © 2024 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on June 10, 2024.
6. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2024 – March 26, 2024). © 2024 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on June 10, 2024.
7. The NCCN Hairy Cell Leukemia Guidelines in Oncology (version 2.2024 – April 22, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 10, 2024.
8. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 1.2025 – November 15, 2024). © 2024 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on December 16, 2024.
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12. The NCCN Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 2.2024 – December 5, 2023). © 2023 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on June 10, 2024.