PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 06/12/2024

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

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 2.2024 – May 22, 2024) recommend Venclexta 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.

- **Venclexta® (venetoclax tablets (AbbVie and Genentech)**

is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

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 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 has chronic myelomonocytic leukemia-2; AND
   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 COVERED

Venclexta® (venetoclax tablets (AbbVie and Genentech) is(are) considered experimental, investigational or unproven for ANY other use(s); 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.
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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 2.2024 – May 22, 2024). © 2024 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on June 10, 2024.
9. The NCCN Myeloproliferative Neoplasms Clinical Practice Guidelines in Oncology (version 1.2024 – December 21, 2023). © 2023 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on June 10, 2024.
10. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 4.2024 – April 26, 2024). © 2024 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on June 10, 2024.
11. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 2.2024 – December 12, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 10, 2024.

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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	07/19/2023
Annual Revision	**Acute Lymphoblastic Leukemia:** Condition of approval and criteria were added to "Other Uses with Supportive Evidence." **Hairy Cell Leukemia:** Condition of approval and criteria were added to "Other Uses with Supportive Evidence." **Mantle Cell Lymphoma**: The following criteria were added as an option for approval, "Patient has a *TP53* mutation and the medication is used as induction therapy in combination with Brukinsa (zanubrutinib) and Gazyva (obinutuzumab intravenous infusion)." **Myelodysplastic Syndrome**. Condition of approval and criteria were added to "Other Uses with Supportive Evidence." **Myeloproliferative Neoplasm:** Condition of approval and criteria were added to "Other Uses with Supportive Evidence."	06/12/2024