PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 06/04/2025

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

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 3.2025 – March 17, 2025) 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 2A/2B).[3]

- **AML**: NCCN guidelines (version 2.2025 – January 27, 2025) 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 2.2025 –February 10, 2025) 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 Stage II-IV (category 2A) in absence of a clinical trial.[5]
- **CLL/SLL**: NCCN guidelines (version 3.2025 – April 2, 2025) cite Venclexta in several scenarios as first-line, second-line, or subsequent line therapy.[6] CLL and SLL are different manifestations of the same disease which are managed similarly.
- **Hairy Cell Leukemia**: NCCN guidelines (version 1.2025 – September 26, 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 2.2025 – January 17, 2025) 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 1.2025 – February 21, 2025) 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 2.2025 – April 11, 2025) recommend Venclexta in combination with other therapies for previously treated relapsed or progressive disease for patients with t (11;14) translocation as "useful in certain circumstances" after 1 to 3 prior therapies (category 2A).[10]

- **Systemic Light Chain Amyloidosis:** NCCN guidelines (version 2.2025 – March 12, 2025) 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 3.2025 – February 6, 2025) 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 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 a 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) The medication 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 a 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 not medically necessary for ANY other use(s).

REFERENCES

1. Venclexta® tablets [prescribing information]. North Chicago, IL and South San Francisco, CA: AbbVie and Genentech; July 2024.
2. The NCCN Pediatric Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 3.2025 – March 17, 2025) © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.
3. The NCCN Acute Lymphoblastic Leukemia Clinical Practice Guidelines in Oncology (version 1.2025 – May 15, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.
4. The NCCN Acute Myeloid Leukemia Clinical Practice Guidelines in Oncology (version 2.2025 – January 27, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.
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 3.2025 – April 2, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 2, 2025.
7. The NCCN Hairy Cell Leukemia Guidelines in Oncology (version 1.2025 – September 26, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.
8. The NCCN Myelodysplastic Syndromes Clinical Practice Guidelines in Oncology (version 2.2025 – January 17, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.
9. The NCCN Myeloproliferative Neoplasms Clinical Practice Guidelines in Oncology (version 1.2025 – February 21, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.
10. The NCCN Multiple Myeloma Clinical Practice Guidelines in Oncology (version 2.2025 – April 11, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 2, 2025.
11. The NCCN Systemic Light Chain Amyloidosis Clinical Practice Guidelines in Oncology (version 2.2025 – March 12, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.

12. The NCCN Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma Clinical Practice Guidelines in Oncology (version 3.2025 – February 6, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on May 30, 2025.

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
Selected Revision	**Myelodysplastic Syndrome**. The following criterion was added as an option for approval, "Patient has higher risk disease" with a note that states "higher risk disease includes patients who have an international prognostic scoring system (IPSS-R) intermediate-, high-, or very-high risk disease".	12/18/2024
Annual Revision	No criteria changes.	06/04/2025