PRIOR AUTHORIZATION POLICY

POLICY: Oncology (Oral – Bruton's Tyrosine Kinase Inhibitor) – Jaypirca Prior Authorization Policy
- Jaypirca® (pirtobrutinib tablets – Eli Lilly)

REVIEW DATE: 06/11/2025; selected revision 06/18/2025 and 12/10/2025

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

Jaypirca, a Bruton's tyrosine kinase (BTK) inhibitor, is indicated for the treatment of the following:[1]

- **Chronic lymphocytic leukemia (CLL) or small lymphocytic leukemia (SLL),** relapsed or refractory in adults who previously been treated with a BTK inhibitor.
- **Mantle cell lymphoma**, relapsed or refractory in adults after at least two lines of systemic therapy, including a BTK inhibitor.

The mantle cell lymphoma indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

Guidelines

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

- **B-Cell Lymphoma**: NCCN guidelines (version 2.2025 – February 10, 2025) discuss mantle cell lymphoma and marginal zone lymphoma.[2,4]
    - **Mantle cell lymphoma**: Brukinsa® (zanubrutinib capsules) and Calquence® (acalabrutinib tablets) [both covalent BTK inhibitors] are cited as "preferred regimens" for second-line and subsequent therapy (both category 2A). Imbruvica® (ibrutinib capsules, tablets and oral suspension) [also a covalent BTK inhibitor], given with or without rituximab, is cited as an "other recommended regimen" for second-line and subsequent therapy (category 2A). Jaypirca, a non-covalent BTK inhibitor, is recommended as a second-line and subsequent therapy for progressive disease after prior covalent BTK inhibitor as "useful in certain circumstances" (category 2A). It is noted that Jaypirca is effective for the management of resistance to covalent BTK inhibitor, including in patients with BTK C481 mutations (which are uncommon in mantle cell lymphoma). Jaypirca can be given as second-line therapy for disease progression during induction or maintenance therapy with covalent BTK inhibitor-based regimens.
    - **Marginal zone lymphoma**: Jaypirca is recommended as a "preferred" non-covalent BTK inhibitor after prior covalent BTK inhibitor as second-line and subsequent therapy for relapsed, refractory, or progressive disease in patients with indications for treatment, including for older or infirm patients with tolerability of combination chemoimmunotherapy is a concern (category 2A).
- **Chronic Lymphocytic Leukemia (CLL)**: NCCN guidelines (version 1.2026 – October 10, 2025) recommend Jaypirca for CLL or SLL with or without del(17p)/TP53 mutation as second-line or subsequent therapy as "preferred" regimen for resistance or intolerance to prior covalent BTK inhibitor (category 2A) and progression while on treatment with a B-cell lymphoma-2 inhibitor (BCL2i)-containing regimen if prior regimen included covalent BTK inhibitor (category 2A). Jaypirca is also listed as "preferred" regimen for relapsed or refractory disease after prior BTK inhibitor and BCL-2 inhibitor regimens (if not previously used) [category 2A]. Jaypirca is also recommended as additional therapy for histologic (Richter) transformation (clonally related or unknown clonal status) as a single agent in untreated CLL at initial diagnosis as additional therapy for partial disease, refractory disease, or progression while on treatment with chemoimmunotherapy regimens or previously treated CLL (category 2A).[3,4]
- **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma:** NCCN guidelines (version 3.2025 – February 6, 2025) recommend Jaypirca for previously treated disease as "useful in certain circumstances" (category 2A).[5]

POLICY STATEMENT

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

- **Jaypirca® (pirtobrutinib tablets - Eli Lilly)**

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 Indication

1. **Chronic Lymphocytic 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 tried at least one Bruton tyrosine kinase (BTK) inhibitor.
   Note: Examples of a BTK inhibitor include: Imbruvica (ibrutinib tablets, capsules, or oral solution), Calquence (acalabrutinib tablets), or Brukinsa (zanubrutinib capsules).

2. **Mantle Cell Lymphoma.** 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 tried at least one systemic chemotherapy regimen; OR
      Note: Examples of a systemic regimen contain one or more of the following products: rituximab, cytarabine, carboplatin, cisplatin, oxaliplatin, cyclophosphamide, doxorubicin, vincristine, methotrexate, bendamustine, Velcade (bortezomib intravenous or subcutaneous injection), and lenalidomide.
      ii. According to the prescriber, patient is not a candidate for a chemotherapy regimen; AND
   C) Patient has tried one Bruton tyrosine kinase inhibitor (BTK) for mantle cell lymphoma.
   Note: Examples of a BTK inhibitors indicated for mantle cell lymphoma include Brukinsa (zanubrutinib capsules), Calquence (acalabrutinib tablets), and Imbruvica (ibrutinib capsules, tablets, and oral suspension).

3. **Small Lymphocytic 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 has tried at least one Bruton tyrosine kinase (BTK) inhibitor.
   Note: Examples of a BTK inhibitor include: Imbruvica (ibrutinib tablets, capsules, or oral solution), Calquence (acalabrutinib tablets), or Brukinsa (zanubrutinib capsules).

Other Uses with Supportive Evidence

4. **Marginal Zone Lymphoma**. Approve for 1 year if the patient meets BOTH of the following (A and B):

Note: Marginal zone lymphoma includes gastric mucosa-associated lymphoid tissue (MALT) lymphoma, non-gastric MALT lymphoma, nodal marginal zone lymphoma, and splenic marginal zone lymphoma.

A) Patient is ≥ 18 years of age; AND

B) Patient has tried at least one Bruton tyrosine kinase (BTK) inhibitor.
Note: Examples of a BTK inhibitor include: Calquence (acalabrutinib tablets), Brukinsa (zanubrutinib capsules), and Imbruvica (ibrutinib tablets, capsules, and oral solution).

5. **Richter's Transformation**. 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 is currently receiving or has tried at least one chemotherapy regimen.
   Note: Examples of a chemotherapy regimen include: EPOCH-R (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, rituximab); HyperCVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine + rituximab, oxaliplatin; OFAR (oxaliplatin, fludarabine, cytarabine, rituximab); RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone); and venetoclax + RCHOP.

6. **Waldenström Macroglobulinemia/Lymphoplasmacytic 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 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, Kyprolis (carfilzomib intravenous infusion), or Ninlaro (ixazomib capsule).

CONDITIONS NOT COVERED

- **Jaypirca® (pirtobrutinib tablets - Eli Lilly)**

is(are) considered not medically necessary for ANY other use(s); criteria will be updated as new published data are available)

REFERENCES

1. Jaypirca® tablets [prescribing information]. Indianapolis, IN: Eli Lilly; December 2025.
2. The NCCN B-Cell Lymphomas Guidelines in Oncology (version 2.2025 – February 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 9, 2025.
3. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2026 – October 10, 2025). © 2025 National Comprehensive Cancer Network. Available at http://www.nccn.org. Accessed on December 5, 2025.
4. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed December 5, 2025. Search term: pirtobrutinib.

5. 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 June 9. 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	**Chronic Lymphocytic Leukemia:** Condition of approval was moved from Other Uses with Supportive Evidence to FDA-Approved Uses section due to new FDA labeling. **Small Lymphocytic Lymphoma:** Condition of approval was moved from Other Uses with Supportive Evidence to FDA-Approved Uses section due to new FDA labeling. **Richter's Transformation to Diffuse Large B-Cell Lymphoma.** New condition of approval and criteria were added to Other Uses with Supportive Evidence section.	12/13/2023
Early Annual Revision	**Marginal Zone Lymphoma:** Condition of approval and criteria were added to Other Uses with Supportive Evidence.	06/19/2024
Selected Revision	**Mantle Cell Lymphoma**: The requirement of trial of at least one systemic regimen was clarified to state at least one systemic "chemotherapy" regimen.	06/26/2024
Update	**04/08/2025**: The policy name was changed from "Oncology - Jaypirca PA Policy" to "Oncology (Oral - Bruton's Tyrosine Kinase Inhibitor) – Jaypirca PA Policy".	--
Annual Revision	**Chronic Lymphocytic Leukemia:** The option for approval which previously stated that "patient has tried Venclexta" was changed to "patient has tried at least one B-cell lymphoma-2 (BCL-2) inhibitor." A note of example of a B-cell lymphoma-2 (BCL-2) inhibitor was added. **Mantle Cell Lymphoma:** The wording of "systemic regimen" was reworded to "chemotherapy regimen" for the option of approval which previously stated "according to the prescriber, patient is not a candidate for a systemic regimen (i.e., an elderly person who is frail)." **Small Lymphocytic Lymphoma:** The option for approval which previously stated that "patient has tried Venclexta" was changed to "patient has tried at least one B-cell lymphoma-2 (BCL-2) inhibitor." A note of example of a B-cell lymphoma-2 (BCL-2) inhibitor was added. **Waldenström Macroglobulinemia/Lymphoplasmacytic Lymphoma:** Condition of approval and criteria were added to Other Uses with Supportive Evidence.	06/11/2025
Selected Revision	**Mantle Cell Lymphoma:** The wording "i.e., an elderly patient who is frail" was removed from the requirement which previously stated, "according to the prescriber, patient is not a candidate for a chemotherapy regimen (i.e., an elderly patient who is frail)."	06/18/2025
Selected Revision	**Chronic Lymphocytic Leukemia:** The option for approval which stated, "patient has resistance or intolerance to Imbruvica (ibrutinib tablets, capsules, or oral solution), Calquence (acalabrutinib tablets), or Brukinsa (zanubrutinib capsules)" was removed. The option for approval which stated that "patient has relapsed or refractory disease" and "patient has tried at least one B-cell lymphoma-2 (BCL-2) inhibitor" along with the Note of examples of B-cell lymphoma-2 (BCL-2) inhibitor was removed. The option for approval which previously stated, "patient has tried a Bruton tyrosine kinase (BTK) inhibitor" was changed to "patient has tried at least one Bruton tyrosine kinase (BTK) inhibitor."	12/10/2025

	Small Lymphocytic Lymphoma: The option for approval which stated, "patient has resistance or intolerance to Imbruvica (ibrutinib tablets, capsules, or oral solution), Calquence (acalabrutinib tablets), or Brukinsa (zanubrutinib capsules)" was removed. The option for approval which stated that "patient has relapsed or refractory disease" and "patient has tried at least one B-cell lymphoma-2 (BCL-2) inhibitor" along with the Note of examples of B-cell lymphoma-2 (BCL-2) inhibitor was removed. The option for approval which previously stated, "patient has tried a Bruton tyrosine kinase (BTK) inhibitor" was changed to "patient has tried at least one Bruton tyrosine kinase (BTK) inhibitor." **Richter's Transformation:** This condition of approval was previously called, "Richter's Transformation to Diffuse Large B-Cell Lymphoma". An option for approval was added for a patient who is currently receiving at least one chemotherapy regimen. The option for approval that the patient is not a candidate for a chemotherapy regimen along with the note of examples of a chemotherapy was removed.	