PRIOR AUTHORIZATION POLICY

POLICY: Oncology – Jaypirca Prior Authorization Policy
- Jaypirca® (pirtobrutinib tablets – Eli Lilly)

REVIEW DATE: 06/19/2024

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 AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. 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 tyrosine kinase (BTK) inhibitor, is indicated for the treatment of:
- Chronic lymphocytic leukemia (CLL) or small lymphocytic leukemia (SLL), in adults who have received at least two prior lines of therapy, including a BTK inhibitor and B-cell lymphoma-2 (BCL-2) inhibitor.
- Mantle cell lymphoma, relapsed or refractory in adults after at least two lines of systemic therapy, including a BTK inhibitor.[1]
  Both indications are 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 2.2024 – April 30, 2024) 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 head-to-head clinical trials in other B-cell malignancies have demonstrated a more favorable toxicity profile for Brukinsa and Calquence compared with Imbruvica without compromising efficacy. Imbruvica + Venclexta® (venetoclax tablets) is cited as "useful in certain circumstances" for second-line and subsequent therapy (category 2A).

- **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 3.2024 – March 26, 2024) recommend Jaypirca for CLL or SLL with or without del(17p)/TP53 mutation as second-line or third-line therapy as "Useful in Certain Circumstances" for resistance or intolerance to prior covalent BTK inhibitor (category 2A). Jaypirca is also listed as "Other Recommended Regimens" for relapsed or refractory disease after prior BTK inhibitor and Venclexta-based regimens (if not previously used) [category 2A]. Jaypirca is also recommended as additional therapy for histologic (Richter) transformation to diffuse large B-cell lymphoma (clonally related or unknown clonal status) as a single agent in patients with del(17p)/TP53 mutation or who are chemotherapy refractory or unable to receive chemoimmunotherapy (category 2A).[3,4]

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 meets ONE of the following (i or ii):
     - **i.** Patient has resistance or intolerance to Imbruvica (ibrutinib tablets, capsules, or oral solution), Calquence (acalabrutinib tablets), or Brukinsa (zanubrutinib capsules); OR
     - **ii.** Patient meets BOTH of the following (a and b):
       - **a)** Patient has relapsed or refractory disease; AND
       - **b)** Patient meets BOTH of the following [(1) and (2)]:
         - **(1)** Patient has tried a Bruton tyrosine kinase (BTK) inhibitor; AND
           Note: Examples of Bruton tyrosine kinase inhibitor include Imbruvica (ibrutinib tablets, capsules, or oral solution), Calquence (acalabrutinib tablets), or Brukinsa (zanubrutinib capsules).
         - **(2)** Patient has tried Venclexta (venetoclax tablet).

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 regimen; OR
  Note: Examples of a systemic regimen contain one or more of the following products: rituximab, dexamethasone, cytarabine, carboplatin, cisplastin, oxaliplatin, cyclophosphamide, doxorubicin, vincristine, prednisone, methotrexate, bendamustine, Velcade (bortezomib intravenous or subcutaneous injection), and lenalidomide.
  ii. According to the prescriber, patient is not a candidate for a systemic regimen (i.e., an elderly patient who is frail); AND
C) Patient has tried one Bruton tyrosine kinase inhibitor (BTK) for mantle cell lymphoma.
Note: Examples of 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 meets ONE of the following (i or ii):
  i. Patient has resistance or intolerance to Imbruvica (ibrutinib tablets, capsules, or oral solution), Calquence (acalabrutinib tablets), or Brukinsa (zanubrutinib capsules); OR
  ii. Patient meets BOTH of the following (a and b):
    a) Patient has relapsed or refractory disease; AND
    b) Patient meets BOTH of the following [(1) and (2)]:
      (1) Patient has tried a Bruton tyrosine kinase (BTK) inhibitor; AND
      Note: Examples of Bruton tyrosine kinase inhibitor include Imbruvica (ibrutinib tablets, capsules, or oral solution), Calquence (acalabrutinib tablets), or Brukinsa (zanubrutinib capsules).
      (2) Patient has tried Venclexta (venetoclax tablet).

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 inhibitor.
Note: Examples of a Bruton tyrosine inhibitor include: Calquence (acalabrutinib tablets), Brukinsa (zanubrutinib capsules), and Imbruvica (ibrutinib tablets, capsules, and oral solution).

5. Richter's Transformation to Diffuse Large B-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 chemotherapy regimen; OR
  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

ii. Patient is not a candidate for a 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

CONDITIONS NOT COVERED

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

is(are) considered experimental, investigational, or unproven for ANY other use(s).

REFERENCES

1. Jaypirca® tablets [prescribing information]. Indianapolis, IN: Eli Lilly; December 2023.
2. The NCCN B-Cell Lymphomas Guidelines in Oncology (version 2.2024 – April 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on June 14, 2024.
3. 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 14, 2024.
4. The NCCN Drugs and Biologics Compendium. © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed June 14, 2024. Search term: pirtobrutinib.

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