Clinical Policy: Pirtobrutinib (Jaypirca)

Reference Number: CP.PHAR.620
Effective Date: 06.01.23
Last Review Date: 05.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Pirtobrutinib (Jaypirca®) is a Bruton tyrosine kinase (BTK) inhibitor.

FDA Approved Indication(s)

Jaypirca is indicated for the treatment of adult patients with:

- Relapsed or refractory mantle cell lymphoma (MCL) after at least two lines of systemic therapy, including a BTK inhbitor.*
- Chronic lymphocytic leukemia or small lymphocytic lymphoma (CLL/SLL) who have received at least two prior lines of therapy, including a BTK inhibitor and a B-cell lymphoma 2 inhibitor (BCL2i).*

**This 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.*

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Jaypirca is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma (must meet all)**:**

1. Diagnosis of CLL or SLL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For Jaypirca requests, member must use pirtobrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. One of the following (a, b, or c):
   a. Member has received ≥ 2 prior lines of therapy (*see Appendix B for examples*) that include both of the following (i and ii):
      i. One BTK inhibitor (e.g., Brukinsa®, Calquence®, Imbruvica®);
      ii. One BCL2i (e.g., Venclexta®);
      **Prior authorization may be required.*
   b. Member has received ≥ 1 prior line of therapy (*see Appendix B for examples*) and has resistance or intolerance to prior covalent BTK inhibitor therapy (e.g., Brukinsa, Calquence, Imbruvica) [off-label];

c. Member has histologic (Richter's) transformation to diffuse large B-cell lymphoma with one of the following (i or ii) [off-label]:
   i. Member has del(17p)/TP53 mutation;
   ii. Member is chemotherapy refractory or unable to receive chemoimmunotherapy;

6. Jaypirca is prescribed as a single agent;
7. Request meets one of the following (a, b, or c):*
   a. Dose does not exceed (i and ii):
      i. 200 mg per day;
      ii. 2 tablets per day;
   b. Request meets both of the following (i and ii):
      i. Dose does not exceed both of the following (1 and 2):
         1) 300 mg per day;
         2) 3 tablets per day;
      ii. Prescriber attestation of member's inability to avoid concomitant use of CYP3A inducer (e.g., carbamazepine, rifampin, ritonavir, St. John's wort);
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

B. Mantle Cell Lymphoma (must meet all)**:**
1. Diagnosis of MCL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For Jaypirca requests, member must use pirtobrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Member has received ≥ 2 prior lines of therapy* (*see Appendix B*);
   **Prior authorization may be required*
6. Member has received prior treatment with a BTK inhibitor (e.g., Imbruvica, Brukinsa, Calquence);
7. Request meets one of the following (a or b):*
   a. Dose does not exceed (i and ii):
      i. 200 mg per day;
      ii. 2 tablets per day;
   b. Request meets both of the following (i and ii):
      i. Dose does not exceed both of the following (1 and 2):
         1) 300 mg per day;
         2) 3 tablets per day;
      ii. Prescriber attestation of member's inability to avoid concomitant use of CYP3A inducer (e.g., carbamazepine, rifampin, ritonavir, St. John's wort);
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:

Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

C. NCCN Compendium Indications (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a or b):
   a. Marginal zone lymphoma (MZL), as subsequent therapy;
   b. Waldenström macroglobulinemia/Lymphoplasmacytic lymphoma, as subsequent therapy;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For Jaypirca requests, member must use pirtobrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. For MZL, member has received prior treatment with a BTK inhibitor (e.g., Imbruvica, Brukinsa, Calquence);
6. Request meets one of the following (a or b):*
   a. Dose does not exceed (i and ii):
      i. 200 mg per day;
      ii. 2 tablets per day;
   b. Request meets both of the following (i and ii):
      i. Dose does not exceed both of the following (1 and 2):
         1) 300 mg per day;
         2) 3 tablets per day;
      ii. Prescriber attestation of member's inability to avoid concomitant use of CYP3A inducer (e.g., carbamazepine, rifampin, ritonavir, St. John's wort);
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line

of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Jaypirca for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Jaypirca requests, member must use pirtobrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed (i and ii):
      i. 200 mg per day;
      ii. 2 tablets per day;
   b. Both of the following (i and ii):
      i. New dose does not exceed both of the following (1 and 2):
         1) 300 mg per day;
         2) 3 tablets per day;
      ii. Prescriber attestation of member's inability to avoid concomitant use of CYP3A inducer (e.g., carbamazepine, rifampin, ritonavir, St. John's wort);
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration:
Medicaid/HIM – 12 months
Commercial – 12 months or duration of request, whichever is less

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BCL2i: B-cell lymphoma 2 inhibitor
BTK: Bruton tyrosine kinase
CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
MCL: mantle cell lymphoma
MZL: marginal zone lymphoma
NCCN: National Comprehensive Cancer Network
SLL: small lymphocytic lymphoma

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of First-Line Treatment Regimens for MCL		
HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone/methotrexate/ cytarabine) + rituximab	Varies	Varies
NORDIC (rituximab + cyclophosphamide, vincristine, doxorubicin, prednisone/rituximab + cytarabine)	Varies	Varies
TRAINGLE regimen: RCHOP + RDHAP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone, ibrutinib)/(rituximab, dexamethasone, cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin)	Varies	Varies
LyMA regimen: RDHAP (rituximab, dexamethasone, cytarabine) + platinum (cisplatin, oxaliplatin, or carboplatin)	Varies	Varies
RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
bendamustine (Bendeka®) + Rituxan® (rituximab)	Varies	Varies
VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)	Varies	Varies
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituxan® (rituximab)	Varies	Varies
lenalidomide (Revlimid®) + Rituxan® (rituximab)	Varies	Varies
RBAC500 (rituximab, bendamustine, cytarabine)	Varies	Varies
Calquence (acalabrutinib) + Rituxan (rituximab)	Varies	Varies
Brukinsa (zanubrutinib)/Gazyva (obinutuzumab)/Venclexta (venetoclax)	Varies	Varies
Examples of Second-Line and Subsequent Therapy for MCL		
BTK inhibitors (Calquence, Brukinsa)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
bendamustine (Bendeka) + rituximab	Varies	Varies
bortezomib (Velcade) ± rituximab	Varies	Varies
DHA (dexamethasone, cytarabine) + platinum (carboplatin, cisplatin, or oxaliplatin) + rituximab	Varies	Varies
GemOx (gemcitabine, oxaliplatin) + rituximab	Varies	Varies
Imbruvica (ibrutinib) + Venclexta (venetoclax)	Varies	Varies
Imbruvica ± rituximab	Varies	Varies
lenalidomide (Revlimid)+ rituximab	Varies	Varies
RBAC500 (rituximab, bendamustine, cytarabine)	Varies	Varies
Venclexta® (venetoclax) ± rituximab	Varies	Varies
CLL/SLL		
Examples of first-line, second-line and subsequent therapies: • FCR (fludarabine, cyclophosphamide, rituximab) • HDMP (high-dose methylprenisolone) + [rituximab or Arzerra® (ofatumumab)] • Calquence (acalabrutinib) ± Gazyva® (obinutuzumab) • Imbruvica (ibrutinib) ± [Gazyva (obinutuzumab) or Venclexta (venetoclax) or Arzerra (ofatumumab) or rituximab] • Brukinsa (zanubrutinib) • Gazyva (obinutuzumab) ± [Venclexta (venetoclax) or Leukeran® (chlorambucil)] • bendamustine + [Arzerra (ofatumumab) or rituximab]	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MCL, CLL, SLL	200 mg PO QD	200 mg/day

VI. Product Availability

Tablets: 50 mg, 100 mg

VII. References

1. Jaypirca Prescribing Information. Indianapolis, IN; Lily USA, LLC: June 2024. Available at: https://jaypirca.lilly.com/. Accessed February 4, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed February 4, 2025.
3. National Comprehensive Cancer Network. B-cell Lymphomas Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed February 4, 2025.

4. Mato AR, Shah NN, Jurczak W, et al. Pirtobrutinib in relapsed or refractory B-cell malignancies (BRUIN): a phase 1/2 study. *Lancet*. 2021 Mar 6; 397(10277): 892-901.
5. Cohen JB, Shah NN, Alencar AJ, et al. MCL-133 Pirtobrutinib, a Highly Selective, Non-Covalent (Reversible) BTK Inhibitor in Previously Treated Mantle Cell Lymphoma: Updated Results From the Phase 1/2 BRUIN Study. *Clin Lymphoma Myeloma Leuk*. 2022 Oct; 22 Suppl 2:S394-S395.
6. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymophoma Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed February 4, 2025.
7. Mato AR, Woyach JA, Brown JR, et al. Pirtobrutinib after a Covalent BTK Inhibitor in Chronic Lymphocytic Leukemia. *N Engl J Med.* 2023 July; 389:33-44.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	02.07.23	05.23
RT4: added new indication for CLL and SLL per updated prescribing information and NCCN supported off-label uses.	12.07.23	
2Q 2024 annual review: for all indications, added maximum dose criteria for concomitant use with CYP3A inducers; updated Appendix B for therapeutic alternatives per NCCN; references reviewed and updated.	02.12.24	05.24
2Q 2025 annual review: added criteria for MZL and waldenstrom macroglobulinemia per NCCN; in Appendix B, updated example therapies per NCCN; references reviewed and updated.	02.04.25	05.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.