Clinical Policy: Acalabrutinib (Calquence)

Reference Number: CP.PHAR.366
Effective Date: 03.01.19
Last Review Date: 02.21
Line of Business: Commercial*, Medicaid

Revision Log

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

Description

Acalabrutinib (Calquence®) is a Bruton tyrosine kinase (BTK) inhibitor.

**For Commercial Exchange Plans,* *this policy applies only when the prescribed agent is on the formulary. Request for non-formulary agents must be reviewed using the formulary exception policy.*

FDA Approved Indication(s)

Calquence is indicated for the treatment of adult patients with:

- Mantle cell lymphoma (MCL) who have received at least one prior therapy*
- Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)

**This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.*

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 Calquence is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. 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 Calquence request, medical justification supports inability to use acalabrutinib, if available, (e.g., contraindications to excipients);
5. Member has received ≥ 1 prior therapy* (*see Appendix B*);
   **Prior authorization may be required*
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (4 capsules) per day;
   b. 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 – 6 months
Commercial – Length of Benefit

B. 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 Calquence request, medical justification supports inability to use acalabrutinib, if available, (e.g., contraindications to excipients);
5. Calquence is prescribed in one of the following ways (a or b):*
   a. First-line therapy as a single agent or in combination with Gazyva®;
   b. Subsequent therapy as a single agent for relapsed or refractory disease, and (i and ii):
      i. Member has received ≥ 1 prior therapy (*see Appendix B*);
      ii. If refractory to Imbruvica®, member does not have a BTK C481S mutation;

   **Prior authorization may be required*
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (4 capsules) per day;
   b. 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 – 6 months
Commercial – Length of Benefit

C. Waldenstrom Macroglobulinemia/Lymphoplasmacytic Lymphoma (off-label) (must meet all)**:**
1. Diagnosis of Waldenstrom macroglobulinemia (WM) or lymphoplasmacytic lymphoma (LPL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For Calquence request, medical justification supports inability to use acalabrutinib, if available, (e.g., contraindications to excipients);
5. Calquence is prescribed as second-line or subsequent therapy;
   **Prior authorization may be required*
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (4 capsules) per day;
   b. 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 – 6 months
Commercial – Length of Benefit

D. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial 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 Calquence for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For Calquence request, medical justification supports inability to use acalabrutinib, if available, (e.g., contraindications to excipients);
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 400 mg (4 capsules) per day;
   b. 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 – 12 months
Commercial – Length of Benefit

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial 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 and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BTK: Bruton tyrosine kinase
CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
LPL: lymphoplasmacytic lymphoma
MCL: mantle cell lymphoma
NCCN: National Comprehensive Cancer Network
SLL: small lymphocytic lymphoma
WM: Waldenstrom macroglobulinemia

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
First-Line Treatment Regimens for MCL		
CALGB (rituximab + methotrexate + cyclophosphophamide, doxorubicin, vincristine, prednisone; etoposide, cytarabine, rituximab; carmustine, etoposide, cyclophosphamide/autologous stem cell rescue; rituximab)	Varies	Varies
HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone/methotrexate/ cytarabine) + rituximab	Varies	Varies
NORDIC (rituximab + cyclophosphamide, vincristine, doxorubicin, prednisone/rituximab + cytarabine)	Varies	Varies
RCHOP/RDHAP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)/(rituximab, dexamethasone, cisplatin, cytarabine)	Varies	Varies
RDHAP (rituximab, dexamethasone, cisplatin, cytarabine)	Varies	Varies
RCHOP/RICE (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)/(rituximab, ifosfamide, carboplatin, etoposide)	Varies	Varies
Bendeka® (bendamustine) + Rituxan® (rituximab)	Varies	Varies
VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)	Varies	Varies
CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + Rituxan® (rituximab)	Varies	Varies
Revlimid® (lenalidomide) + Rituxan® (rituximab)	Varies	Varies
First-Line Treatment Regimens for CLL/SLL		
Without del(17p)/TP53 mutation		
Leukeran® (chlorambucil) + Gazyva® (obinutuzumab)	Varies	Varies
Imbruvica® (ibrutinib)	Varies	Varies
Leukeran® (chlorambucil) + Rituxan® (rituximab)	Varies	Varies
bendamustine (Bendeka®, Treanda®) + CD20 monoclonal antibody (e.g., rituximab, ofatumumab, obinutuzumab)	Varies	Varies
FR/FCR (fludarabine, rituximab ± cyclophosphamide)	Varies	Varies
Venclexta® (venetoclax) + Gazyva® (obinutuzumab)	Varies	Varies
With del(17p)/TP53 mutation		
Imbruvica® (ibrutinib)	Varies	Varies
Venclexta® (venetoclax) + Gazyva® (obinutuzumab)	Varies	Varies
Campath® (alemutuzumab) ± Rituxan® (rituximab)	Varies	Varies
High-dose methylprednisolone + Rituxan® (rituximab)	Varies	Varies
Gazyva® (obinutuzumab)	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

Appendix D: General Information
Due to lack of activity, Calquence should not be used for ibrutinib-refractory CLL cells with BTK C481S mutations. Calquence can, however, be used in cases of ibrutinib intolerance. [NCCN: CLL/SLL guidelines.]

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
MCL	100 mg PO BID	400 mg/day
CLL/SLL	Monotherapy: 100 mg PO BID Calquence in combination with Gazyva for patients with previously untreated CLL/SLL: Start Calquence 100 mg PO BID at Cycle 1 (each cycle is 28 days). Start Gazyva at Cycle 2 for a total of 6 cycles. Administer Calquence prior to Gazyva when given on the same day.	400 mg/day

VI. Product Availability
Capsule: 100 mg

VII. References
1. Calquence Prescribing Information. Wilmington, DE; AstraZeneca Pharmaceuticals LP: November 2019. Available at: www.calquence.com. Accessed November 9, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 9, 2020.
3. National Comprehensive Cancer Network. B-cell Lymphomas Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed Novemberber 9, 2020.
4. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed November 9, 2020.
5. National Comprehensive Cancer Network. Waldenstrom Macroglobulinemia / Lymphoplasmacytic Lymphoma Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed November 9, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	12.05.17	02.18
1Q19 annual review: added age requirement for MCL; added hematologist as a prescriber option for MCL; criteria added for 2A NCCN-supported off-label use in CLL/SLL; references reviewed and updated.	11.06.18	02.19
1Q 2020 annual review: RT2: Updated criteria to reflect new FDA approved indication of CLL/SLL for Calquence therapy used in	01.07.20	02.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
combination with or without Gazyva; references reviewed and updated.; references reviewed and updated.		
1Q 2021 annual review: oral oncology generic redirection language added; WM/LPL added per NCCN; references reviewed and updated.	11.09.20	02.21

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.