Clinical Policy: Acalabrutinib (Calquence)

Reference Number: CP.PHAR.366
Effective Date: 03.01.19
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

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

FDA Approved Indication(s)

Calquence is indicated:

- In combination with bendamustine and rituximab for the treatment of adult patients with previously untreated mantle cell lymphoma (MCL) who are ineligible for autologous hematopoietic stem cell transplantation (HSCT)
- For the treatment of adult patients with MCL who have received at least one prior therapy
- For the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)

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 requests, member must use generic acalabrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Member does not have Imbruvica®-refractory MCL with BTK C481S mutations;
6. Member meets one of the following (a or b):
   a. Received ≥ 1 prior therapy* (*see Appendix B*);
   b. Member meets one of the following (i, ii, or iii):
      i. Prescribed in combination with bendamustine and rituximab, and member is ineligible for autologous HSCT;
      ii. Prescribed in combination with rituximab for less aggressive induction therapy;
      iii. Prescribed in combination with rituximab as pretreatment in order to limit the number of cycles of aggressive induction therapy with RHyperCVAD (ritixumab, cyclophosphamide, vincristine, doxorubicin, and dexamethasone);

**Prior authorization may be required*

7. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (4 capsules or 4 tablets) 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/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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 requests, member must use generic acalabrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced ;
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 (i.e., member has received ≥ 1 prior therapy (*see Appendix B*)) as a single agent for relapsed or refractory disease;

   **Prior authorization may be required*
6. Member does not have Imbruvica-refractory CLL/SLL with BTK C481S mutations;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (4 capsules or 4 tablets) 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/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

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 requests, member must use generic acalabrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Calquence is prescribed as a single agent as second-line or subsequent therapy;

   **Prior authorization may be required*
6. Calquence is not prescribed concurrently with Imbruvica or Brukinsa;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (4 capsules or 4 tablets) 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/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

D. Marginal Zone Lymphoma (*B-cell lymphoma subtype*) (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. Nodal MZL for relapsed, refractory, or progressive disease;
   b. Splenic MZL;
   c. Extranodal MZL (noncutaneous) for relapsed, refractory, or progressive disease;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For Calquence requests, member must use generic acalabrutinib, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Member has received ≥ 1 prior therapy;
6. Calquence is not prescribed concurrently with Imbruvica or Brukinsa;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed 400 mg (4 capsules or 4 tablets) 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/HIM – 6 months
Commercial – 12 months or duration of request, whichever is less

E. 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 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 requests, member must use generic acalabrutinib, 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 400 mg (4 capsules or 4 tablets) 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/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

BTK: Bruton tyrosine kinase
CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
HSCT: hematopoietic stem cell transplantation
LPL: lymphoplasmacytic lymphoma

MALT: mucosa-associated lymphoid tissue
MCL: mantle cell lymphoma
MZL: marginal zone 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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/SLL or MCL with BTK C481S mutations. For CLL/SLL only, however, Calquence can be used in cases of ibrutinib intolerance. [NCCN: CLL/SLL and MCL 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

- Tablet: 100 mg
- Capsule: 100 mg

VII. References

1. Calquence Tablet Prescribing Information. Wilmington, DE; AstraZeneca Pharmaceuticals LP: January 2025. Available at: www.calquence.com. Accessed January 23, 2025.
2. Calquence Capsule Prescribing Information. Wilmington, DE; AstraZeneca Pharmaceuticals LP: January 2025. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/216387Orig2s000Correctedlbl.pdf . Accessed January 23, 2025.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 23, 2025.
4. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed December 2, 2024.

5. National Comprehensive Cancer Network. B-cell Lymphomas Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed January 23, 2025.
6. National Comprehensive Cancer Network. Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma Version 1.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed December 2, 2024.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: oral oncology generic redirection language added; WM/LPL added per NCCN; references reviewed and updated.	11.09.20	02.21
1Q 2022 annual review: added criteria for lack of BTK C481S mutation if refractory to Imbruvica for MCL per NCCN; added off-label criteria for B-cell lymphomas per NCCN; clarified oral oncology generic redirection language to "must use"; added legacy Wellcare auth durations (WCGCP.PHAR.366 to retire); clarified definition of refractory within MCL and CLL/SLL criteria; references reviewed and updated.	11.09.21	02.22
Revised approval duration for Commercial line of business from length of benefit to 12 months or duration of request, whichever is less	01.20.22	05.22
RT4: added newly approved tablet formulation; consolidated Legacy WellCare approval durations to standard Medicaid approval durations of 6/12 months. Template changes applied to other diagnoses/indications.	08.26.22	
Per August SDC, added HIM line of business, removed the following for MCL, CLL, and SLL indications: "If refractory to Imbruvica® (member previously used Imbruvica and remission was not achieved or disease stopped responding), member does not have a BTK C481S mutation"; for WM, LPL, and MZL added requirement that Calquence is not prescribed concurrently with Imbruvica or Brukinsa; for MZL, clarified non-gastric MALT is noncutaneous and added Nodal MZL per NCCN.	08.23.22	11.22
1Q 2023 annual review: no significant changes; references reviewed and updated.	11.17.22	02.23
1Q 2024 annual review: no significant changes; per NCCN recommendations, clarified that Calquence is not to be used in Imbruvica-refractory CLL/SLL that has BTK C481S mutations, and removed the requirement that Imbruvica be tried first before Calquence for MZL (Imbruvica has lost its FDA approval for this indication); references reviewed and updated.	11.28.23	02.24
1Q 2025 annual review: per NCCN guidelines added use as induction or maintenance therapy or use as pretreatment for MCL, for WM clarified that Calquence is to be used as a single agent,	01.23.25	02.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
replaced the terms "Gastric and Nongastric MALT lymphoma" with "Extranodal MZL (noncutaneous)" to align with NCCN nomenclature, for Nodal and Extranodal MZL added the requirement for relapsed, refractory, or progressive disease; references reviewed and updated. RT4 update: added newly FDA-approved indication for first-line use in MCL and converted previous accelerated approval for second-line use in MCL to full approval; per NCCN guidelines removed use of Calquence as maintenance therapy for MCL (category 2B rec); revised use of Calquence as induction therapy for MCL to specify use in combination with rituximab and only for less aggressive induction therapy (as opposed to aggressive induction therapy which is a category 2B rec); added exclusion for Imbruvica-refractory MCL with BTK C481S mutations; removed the Legacy Wellcare auth duration for initial approval of the MCL indication and consolidated to the standard Medicaid approval duration of 6 months.		

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.