Clinical Policy: Acalabrutinib (Calquence)

Reference Number: ERX.SPA.224
Effective Date: 03.01.19
Last Review Date: 02.22
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.

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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 acalabrutinib, if available unless contraindicated or clinically significant adverse effects are experienced;
5. Member has received ≥ 1 prior therapy* (*see Appendix B*);
   **Prior authorization may be required*
6. 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;
7. 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:
Commercial – Length of Benefit
Medicaid – 6 months

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 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 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 previously used Imbruvica, and remission was not achieved or disease stopped responding), member does not have BTK C481S mutations;

   **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:
Commercial – Length of Benefit
Medicaid – 6 months

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 acalabrutinib, if available unless contraindicated or clinically significant adverse effects are experienced;
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:
Commercial – Length of Benefit
Medicaid – 6 months

D. B-Cell Lymphomas (off-label) (must meet all)**:**
1. Diagnosis of one of the following (a, b, or c):
   a. Splenic marginal zone lymphoma;
   b. Gastric MALT lymphoma;
   c. Nongastric MALT lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For Calquence requests, member must use acalabrutinib, if available unless contraindicated or clinically significant adverse effects are experienced;
5. Member has received ≥ 1 prior therapy;
6. Member has intolerance or contraindication to Imbruvica;
7. 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:
Commercial – Length of Benefit
Medicaid – 6 months

E. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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 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) 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:
Commercial – Length of Benefit
Medicaid – 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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
MALT: mucosa-associated lymphoid tissue
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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
First-Line Treatment Regimens for MCL		
CALGB (rituximab + methotrexate + cyclophosphosphamide, 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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:	400 mg/day

Indication	Dosing Regimen	Maximum Dose
	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.	

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, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 9, 2021.
3. National Comprehensive Cancer Network. B-cell Lymphomas Version 5.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed November 9, 2021.
4. National Comprehensive Cancer Network. Waldenstrom Macroglobulinemia / Lymphoplasmacytic Lymphoma Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed November 9, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	12.05.17	02.18
1Q 2019 annual review: added age requirement for MCL; added hematologist as a prescriber option for MCL; criteria added for NCCN-supported off-label use in CLL/SLL; references reviewed and updated.	10.30.18	02.19
1Q 2020 annual review: RT2: Updated criteria to reflect new FDA approved indication of CLL/SLL for Calquence therapy used in combination with or without Gazyva; references reviewed and updated; references reviewed and updated.	01.07.20	02.20
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”; clarified definition of refractory within MCL and CLL/SLL criteria; references reviewed and updated.	11.09.21	02.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.

be bound by the foregoing terms and conditions, in addition to the Site Use Agreement for Health Plans associated with Envolve Pharmacy Solutions.