



PHARMACY COVERAGE GUIDELINES  
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 1/18/18  
LAST REVIEW DATE: 1/18/18  
LAST CRITERIA REVISION DATE:  
ARCHIVE DATE:

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## CALQUENCE® (acalabrutinib) oral capsule

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Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

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This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy).

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com). **Incomplete forms or forms without the chart notes will be returned.**

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## **CALQUENCE® (acalabrutinib) oral capsule (cont.)**

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### **Description:**

Calquence (acalabrutinib) is a bruton tyrosine kinase inhibitor (BTKI) indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. 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.

Bruton tyrosine kinase (BTK) is a signaling molecule that activates B-cell proliferation, trafficking, chemotaxis, and adhesion. Calquence (acalabrutinib) binds with BTK active site, leading to inhibition of BTK enzymatic activity.

### **Background:**

- Mantle cell lymphoma (MCL) is a rare, fast growing form of mature B-cell non-Hodgkin lymphomas (NHL)
- MCL has been previously referred to as intermediate lymphocytic lymphoma, mantle zone lymphoma, centrocytic lymphoma, and lymphocytic lymphoma of intermediate differentiation
- MCL encompasses approximately 3-10% of adult NHLs in the US
- The histologic pattern of MCL may be diffuse, nodular, or mantle zone, or a combination
- The course of MCL is moderately aggressive and variable
- Most patients present with advanced stage disease with disease spread to lymph nodes, bone marrow, and other organs
- Combination chemotherapy plus immunotherapy remains the main treatment modality with or without high-dose therapy and autologous hematopoietic cell transplantation
- Initially, all patients with MCL should receive rituximab in addition to chemotherapy
- A number of treatment regimens have been evaluated in patients with recurrent or refractory MCL
- Choice is primarily made based on the patient's prior treatment, comorbidities and performance status, expected toxicities, and the clinician's experience with the regimens

### **Usual Therapy:**

***National Comprehensive Cancer Network Guideline: B-Cell Lymphoma version 7.2017 (12/05/2017)  
Category 2A suggested regimens, unless otherwise stated (alphabetical order)***

#### *Aggressive therapy:*

- CALGB (treatment 1, 2, 2.5: rituximab, methotrexate with augmented CHOP, treatment 3: etoposide, cytarabine, rituximab, treatment 4: carmustine, etoposide, cyclophosphamide/autologous stem cell rescue, treatment 5: rituximab maintenance) Treatment 2.5 is given if the pre-treatment bone marrow biopsy contains > 15% MCL)
- HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone alternating with high-dose methotrexate and cytarabine) + rituximab

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## CALQUENCE® (acalabrutinib) oral capsule (cont.)

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- NORDIC (dose-intensified induction immunochemotherapy with rituximab, cyclophosphamide, vincristine, doxorubicin, prednisone [maxi-CHOP]) alternating with rituximab, high-dose cytarabine)
- Alternating RCHOP / RDHAP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) / (rituximab, dexamethasone, cisplatin, cytarabine)
- RDHAP (oxaliplatin or carboplatin can be used instead of cisplatin)
- Sequential RCHOP / RICE (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) / (rituximab, ifosfamide, carboplatin, etoposide)

*Less aggressive therapy:*

- Bendamustine + rituximab
- VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, prednisone)
- CHOP + rituximab
- Lenalidomide + rituximab
- Modified rituximab-HyperCVAD in patients > 65 years (rituximab + ibrutinib can be used as a pre-treatment to limit the number of cycles of RHyperCVAD/rituximab maintenance)

*First-line consolidation candidate for HDT/ASCR:*

- High-dose therapy with autologous stem cell rescue + rituximab maintenance (category 1 for rituximab maintenance)

*First-line consolidation not a candidate for HDT/ASCR:*

- Rituximab maintenance (category 1 following RCHOP)

*Second-line therapy:*

- Acalabrutinib
- Bendamustine ± rituximab
- Bortezomib ± rituximab
- Cladribine + rituximab
- Ibrutinib
- Lenalidomide ± rituximab
- Venetoclax

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*Second-line consolidation:*

- Allogeneic stem cell transplant (non-myeloablative or myeloablative)
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## Calquence (acalabrutinib)

### Medication class:

Antineoplastic Agent, Bruton Tyrosine Kinase Inhibitor

### FDA-approved indication(s):

- Treatment of mantle cell lymphoma (MCL) in patients who have received at least 1 prior therapy

### Limitations of use:

- 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

### Recommended Dose:

- 100 mg twice daily

#### **Maximum dosage**

- Not stated, but label states that when used with a strong CYP 3A4 inducer, the dose of Calquence should be increased to 200 mg twice daily

### Available Dosage Forms:

- 100 mg capsules

### Warnings, Precautions, and other Clinical Information:

- Calquence (acalabrutinib) has not been evaluated in patients with severe hepatic impairment (Child-Pugh Class C or total bilirubin between 3-10x ULN and any AST)
- Monitor for bleeding and manage appropriately
- Monitor patients for signs and symptoms of infection and treat as needed, consider prophylaxis in patients at risk for opportunistic infections
- Infections due to hepatitis B virus reactivation and progressive multifocal leukoencephalopathy (PML) have occurred
- Monitor complete blood counts monthly for thrombocytopenia and neutropenia
- Secondary primary malignancy can occur, especially skin cancer, advise patients to use sun protection
- Interrupt and reduce Calquence dose with third occurrence of an adverse effect
- Discontinue Calquence with fourth occurrence of an adverse reaction
- Avoid use with strong CYP3A inhibitor, if inhibitor use is to be  $\leq 7$  days, interrupt dose of Calquence
- With moderate CYP3A inhibitor use, reduce Calquence dose to 100 mg once daily
- Avoid use with strong CYP3A inducers, if unable to avoid, adjust dose of Calquence to 200 mg twice daily
- Avoid use with proton pump inhibitors, separation of doses does not eliminate the interaction
- Stagger dosing with H2-receptor antagonists and antacids
- Woman who is breast feeding an infant or child should stop breast feeding
- The mean absolute bioavailability of Calquence (acalabrutinib) is 25%, solubility decreases with increasing pH

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## CALQUENCE® (acalabrutinib) oral capsule (cont.)

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### Criteria:

- **Criteria for initial therapy:** Calquence (acalabrutinib) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:

1. Prescriber is an Oncologist
2. Individual is 18 years of age or older
3. A confirmed diagnosis of mantle cell lymphoma (MCL)
4. Individual has received at least **ONE** prior therapy
  - See NCCN Category 2A list in Description section

**Initial approval duration:** 6 months

- **Criteria for continuation of coverage (renewal request):** Calquence (acalabrutinib) is considered *medically necessary* and will be approved when **ALL** of the following criteria are met:

1. Individual continues to be seen by an Oncologist
2. Individual's condition has not worsened while on therapy
  - Worsening is defined as:
    - Cancer progression
3. Individual has been adherent with the medication
4. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
  - Significant adverse effect such as:
    - Hemorrhage
      - Signs and symptoms may include: blood in stool, dark red or tar-like stools, coughing up blood, vomiting blood, or unusual bleeding, easy bruising, blood in urine, dizziness or feeling faint
    - Thrombocytopenia/neutropenia
      - Signs and symptoms may include: bleeding and easy bruising, unusual bleeding or bruising, nose bleeds, red or purple spots on body, fever, signs of infection
    - Progressive multifocal leukoencephalopathy (PML)
      - Signs and symptoms may include: mental deterioration, vision loss, speech disturbances, ataxia, paralysis, coma, and seizures
5. There are no significant interacting drugs

**Renewal duration:** 12 months

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### Resources:

Off Label Use of Cancer Medications: A.R.S. §§ 20-826(R) & (S). Subscription contracts; definitions.

Off Label Use of Cancer Medications: A.R.S. §§ 20-1057(V) & (W). Evidence of coverage by health care service organizations; renewability; definitions.

Calquence (acalabrutinib). Package Insert. Revised by manufacturer 10-2017. Accessed 01-05-2018.

NCCN Clinical Practice Guidelines in Oncology: B-cell Lymphomas. Version 7.2017, Dec 5, 2017.  
[https://www.nccn.org/professionals/physician\\_gls/pdf/b-cell.pdf](https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf)

UpToDate: Treatment of relapsed or refractory mantle cell lymphoma. Current through Dec 2017. [https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-relapsed-or-refractory-mantle-cell-lymphoma?search=mantle%20cell%20lymphoma&source=search\\_result&selectedTitle=3~70&usage\\_type=default&display\\_rank=3](https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-relapsed-or-refractory-mantle-cell-lymphoma?search=mantle%20cell%20lymphoma&source=search_result&selectedTitle=3~70&usage_type=default&display_rank=3)

UpToDate: Initial treatment of mantle cell lymphoma. Current through Dec 2017. [https://www-uptodate-com.mwu.idm.oclc.org/contents/initial-treatment-of-mantle-cell-lymphoma?search=mantle%20cell%20lymphoma&source=search\\_result&selectedTitle=2~70&usage\\_type=default&display\\_rank=2](https://www-uptodate-com.mwu.idm.oclc.org/contents/initial-treatment-of-mantle-cell-lymphoma?search=mantle%20cell%20lymphoma&source=search_result&selectedTitle=2~70&usage_type=default&display_rank=2)

UpToDate: Clinical manifestations, pathologic features, and diagnosis of mantle cell lymphoma. Current through Dec 2017. [https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-manifestations-pathologic-features-and-diagnosis-of-mantle-cell-lymphoma?search=mantle%20cell%20lymphoma&source=search\\_result&selectedTitle=1~70&usage\\_type=default&display\\_rank=1#H15](https://www-uptodate-com.mwu.idm.oclc.org/contents/clinical-manifestations-pathologic-features-and-diagnosis-of-mantle-cell-lymphoma?search=mantle%20cell%20lymphoma&source=search_result&selectedTitle=1~70&usage_type=default&display_rank=1#H15)

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Fax completed prior authorization request form to 602-864-3126 or email to [pharmacyprecert@azblue.com](mailto:pharmacyprecert@azblue.com).  
 Call 866-325-1794 to check the status of a request.  
 All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**  
 Pharmacy Coverage Guidelines are available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy).

# Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.

**REQUIRED:** Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information			
Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information			
Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information		
Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information			
Medication Name:	Strength:	Dosage Form:	
Directions for Use:	Quantity:	Refills:	Duration of Therapy/Use:

Check if requesting **brand** only     Check if requesting **generic**

Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review	
<input type="checkbox"/> Standard <input type="checkbox"/> Urgent. Sign here: _____	<input type="checkbox"/> Exigent (requires prescriber to include a written statement)

Clinical Information	
1. What is the diagnosis? Please specify below. ICD-10 Code: _____ Diagnosis Description: _____	
2. <input type="checkbox"/> Yes <input type="checkbox"/> No    Was this medication started on a recent hospital discharge or emergency room visit?	
3. <input type="checkbox"/> Yes <input type="checkbox"/> No    There is absence of ALL contraindications.	

4. What medication(s) has the individual tried and failed for this diagnosis? Please specify below.  
 Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. Are there any supporting labs or test results? Please specify below.

Date	Test	Value

# Pharmacy Prior Authorization Request Form

**6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.**  
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

**Signature affirms that information given on this form is true and accurate and reflects office notes**

Prescribing Provider's Signature: \_\_\_\_\_ Date: \_\_\_\_\_

**Please note:** Some medications may require completion of a drug-specific request form.

**Incomplete forms or forms without the chart notes will be returned.**

Office notes, labs, and medical testing relevant to the request that show medical justification are required.