BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 01/18/18**
SECTION: DRUGS	**LAST REVIEW DATE: 02/21/19**
	LAST CRITERIA REVISION DATE: 02/21/19
	ARCHIVE DATE:

CALQUENCE® (acalabrutinib) oral capsule

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.

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.

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

CALQUENCE® (acalabrutinib) oral capsule (cont.)

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 **ONE** of the following:
     - Mantle cell lymphoma (MCL) as single agent second-line therapy after a partial response to induction therapy or for relapsed or progressive disease
     - Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma for relapsed or refractory disease with or without del(17p)/TP53 mutation as a single agent in patients with indications for treatment **and** will not be used for ibrutinib refractory CLL/SLL in patients with BTK C481S mutations
     - Other request for a specific oncologic direct treatment use that is found and listed in the National Comprehensive Cancer Network (NCCN) Guidelines with Categories of Evidence and Consensus of 1 and 2A

  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
       - Thrombocytopenia/neutropenia
       - Progressive multifocal leukoencephalopathy (PML)

  5. There are no significant interacting drugs

  Renewal duration: 12 months

CALQUENCE® (acalabrutinib) oral capsule (cont.)

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)

CALQUENCE® (acalabrutinib) oral capsule (cont.)

- HyperCVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone alternating with high-dose methotrexate and cytarabine) + rituximab
- 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

CALQUENCE® (acalabrutinib) oral capsule (cont.)

- Venetoclax

Second-line consolidation:
- Allogeneic stem cell transplant (non-myeloablative or myeloablative)

Resources:

NCCN Drugs & Biologics Compendium Calquence accessed 02-01-19

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

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

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

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

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Fax completed prior authorization request form to 602-864-3126 or email to 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.

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

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ 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

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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.