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Section:	Prescription Drugs	**Effective Date:**	January 1, 2023
Subsection:	Antineoplastic Agents	**Original Policy Date:**	November 17, 2017
Subject:	Calquence	**Page:**	1 of 5

Last Review Date: December 2, 2022

Calquence

Description

Calquence (acalabrutinib)

Background
Calquence (acalabrutinib) is a small-molecule inhibitor of Bruton tyrosine kinase (BTK). Calquence and its active metabolite, ACP-5862, form a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK enzymatic activity. BTK is a signaling molecule of the B cell antigen receptor (BCR) and cytokine receptor pathways. In B cells, BTK signaling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion. As a result of BTK inhibition, Calquence inhibits malignant B-cell proliferation and tumor growth (1-2).

Regulatory Status
FDA-approved indications: Calquence is a kinase inhibitor indicated for the treatment of adult patients with: (1-2)

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

Calquence used in combination with obinutuzumab is only indicated for previously untreated CLL or SLL (1-2).

Patients have a chance of Grade 3 or higher bleeding events (subdural hematoma, gastrointestinal bleeding, and hematuria). Calquence may increase the risk of hemorrhage in patients receiving antiplatelet or anticoagulant therapies. Consider the benefit-risk of withholding

Calquence for at least 3 to 7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding (1-2).

Significant adverse reactions may occur with Calquence therapy including fatal and non-fatal infections, atrial fibrillation, atrial flutter, cytopenias, myelosuppression and primary malignancies including skin cancers. Patients should have the following monitored while on Calquence therapy: fever, infections, complete blood counts, and hydration (1-2).

Based on findings in animals, Calquence may cause fetal harm when administered to a pregnant woman (1-2).

The safety and effectiveness of Calquence in pediatric patients have not been established (1-2).

Related policies
Brukinsa, Imbruvica

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Calquence may be considered **medically necessary** in patients who are 18 years of age or older with mantle cell lymphoma (MCL) or chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) and if the conditions indicated below are met.

Calquence may be considered **investigational** in patients who are less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have **ONE** of the following:

1. Mantle cell lymphoma (MCL)
    a. Patient has received at least one prior therapy

b. Used as a single agent

2. Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
   a. **AND ONE** of the following:
      i. Used as a single agent
      ii. Used in combination with Gazyva (obinutuzumab) as first-line therapy for CLL or SLL

AND ALL of the following for **BOTH** indications:
- a. Prescriber agrees to do a baseline CBC and monitor monthly during therapy
- b. Prescriber agrees to monitor for malignancies
- c. Prescriber agrees to monitor for bleeding

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have **ONE** of the following:

1. Mantle cell lymphoma (MCL)
2. Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)

AND ALL of the following for **BOTH** indications:
- a. Prescriber agrees to monitor CBC monthly during therapy
- b. Prescriber agrees to monitor for malignancies
- c. Prescriber agrees to monitor for bleeding
- d. **NO** disease progression or unacceptable toxicity

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity	100 mg	180 units per 90 days
Duration	12 months	

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Calquence (acalabrutinib) is a small-molecule inhibitor of BTK. Calquence and its active metabolite, ACP-5862, form a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK enzymatic activity. BTK is a signaling molecule of the B cell antigen receptor (BCR) and cytokine receptor pathways. In B cells, BTK signaling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion. As a result of BTK inhibition, Calquence inhibits malignant B-cell proliferation and tumor growth. The safety and effectiveness of Calquence in pediatric patients have not been established (1-2).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Calquence while maintaining optimal therapeutic outcomes.

References

1. Calquence capsules [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; November 2019.
2. Calquence tablets [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; August 2022.
3. NCCN Drugs & Biologics Compendium® Acalabrutinib 2022. National Comprehensive Cancer Network, Inc. Accessed on October 7, 2022.

Policy History

Date	Action
November 2017	New addition to PA

March 2018	Annual editorial review and reference update Addition of relapsed or refractory chronic lymphocytic leukemia (CLL) /small lymphocytic lymphoma (SLL) with no prior therapy with ibrutinib (Imbruvica) in patients with BTK C481S mutations per SME Addition of the following requirements: used as a single agent, prescriber agrees to do a baseline CBC and monitor monthly during therapy, prescriber agrees to monitor for malignancies, and prescriber agrees to monitor for bleeding per SME
June 2018	Annual review
June 2019	Annual review and reference update
December 2019	Revised indication for CLL/SLL: no longer has to be relapsed or refractory and no prior therapy required
March 2020	Annual review. Revised CLL/SLL indication to be first-line therapy if used in combination with Gazyva
June 2020	Annual review
March 2021	Annual editorial review
March 2022	Annual review and reference update
September 2022	Changed quantity limit to 180 units per 90 days for the addition of Calquence tablets
December 2022	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 2, 2022 and is effective on January 1, 2023.