acalabrutinib (Calquence®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO108

Description

Acalabrutinib (Calquence) and its active metabolite inhibit Bruton tyrosine kinase (BTK) by irreversibly bonding to the active BTK site. This prevents activation of the signaling proteins CD86 and CD69, as well as inhibits proliferation and survival of malignant B cells.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Dosage Form	Indication	Quantity Limit
acalabrutinib (Calquence)	100 mg capsule	Mantle cell lymphoma (previously treated); Chronic lymphocytic leukemia (CLL); small lymphocytic lymphoma (SLL)	60 capsules/30 days

Initial Evaluation

I. Acalabrutinib (Calquence) may be considered medically necessary when the following criteria below are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an oncologist or hematologist; **AND**
   C. Member has <u>not</u> experienced disease progression while on a BTK inhibitor [e.g. zanubrutinib (Brukinsa®), ibrutinib (Imbruvica®)]; **AND**
   D. A diagnosis of one of the following:
      1. **Mantle cell lymphoma (MCL)**; **AND**
         i. Treatment with least one first-line therapy for MCL [e.g., rituximab, bendamustine + rituximab, CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) - based regimen, Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone), bortezomib or carfilzomib, stem-cell transplant, lenalidomide, etc.] has been ineffective, contraindicated, or not tolerated; **OR**
      2. **Chronic Lymphocytic Leukemia (CLL) or small lymphocytic lymphoma (SLL)**; **AND**
         i. Medication is used in **<u>one</u>** of the following settings:
            a. Previously untreated CLL/SLL; **AND**

i. Medication will be used as monotherapy or in combination with obinutuzumab (Gazyva); **OR**

b. Relapsed or refractory after at least one prior systemic therapy; **AND**

i. Member has **not** experienced disease progression while on venetoclax (Vencelxta) or a phosphoinositide-3 kinase inhibitor [e.g. duvelisib (Copiktra), idelalisib (Zydelig)]; **AND**

ii. Medication will **not** be used in combination with other oncologic medications (i.e., will be used as monotherapy)

II. Acalabrutinib (Calquence) is considered investigational when used for all other conditions, including but not limited to:

A. Diffuse Large B-Cell Lymphoma
B. Head and neck squamous cell carcinoma
C. Ovarian cancer
D. Non-small cell lung cancer (NSCLC)
E. Severe Chronic Graft Versus Host Disease
F. Waldenström's macroglobulinemia (WM)

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. Initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. The medication is prescribed by, or in consultation with, an oncologist; **AND**
IV. Medication will **not** be used in combination with other oncologic medications (i.e., will be used as monotherapy); **OR**
    A. Acalabrutinib (Calquence) will be used in combination with obinutuzumab (Gazyva) in the setting of previously untreated CLL/SLL; **AND**
V. Documentation is provided indicating disease response to therapy, as defined by: stabilization of disease, decrease in the size of the tumor, or tumor spread.

Supporting Evidence

I. Safety and efficacy of acalabrutinib (Calquence) has not been established in the pediatric population.
II. MCL, CLL, and SLL are difficult, life threatening diseases, accordingly treatment with acalabrutinib (Calquence) requires consultation with an oncologist or hematologist.
III. There is no published data from a head-to-head studies between acalabrutinib (Calquence) and other BTK inhibitors [zanubrutinib (Brukinsa), ibrutinib (Imbruvica)] to show superiority of one BTK inhibitor over another. There is also no published data in the use of BTK inhibitors in

patients diagnosed with MCL or CLL/SLL that have relapsed or are refractory to other BTK inhibitors. Additionally, no data is available to show one BTK inhibitor could overcome common mechanisms of resistance of BTK inhibitors.

IV. Acalabrutinib (Calquence) was studied in an open-label, phase 2 study in patients with relapsed or refractory mantle cell lymphoma. Oral acalabrutinib (100 mg twice per day) was given until disease progression or unacceptable toxicity. The most common prior therapies in clinical trials included rituximab, bendamustine + rituximab, CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) - based regimen, Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone), bortezomib or carfilzomib, stem-cell transplant and lenalidomide.

V. The efficacy of acalabrutinib (Calquence) in patients with CLL was demonstrated in two randomized, controlled trials which included patients with SLL because it is the same disease. In the ELEVATE-TN trial, a randomized, multicenter, open-label, actively controlled, 3 arm trial of acalabrutinib in combination with obinutuzumab, acalabrutinib monotherapy, and obinutuzumab in combination with chlorambucil in patients with previously untreated chronic lymphocytic leukemia, both the acalabrutinib (Calquence) monotherapy arm and acalabrutinib (Calquence) in combination with obinutuzumab arm significantly prolonged progression free survival (PFS) when compared to obinutuzumab plus chlorambucil.

VI. The efficacy of acalabrutinib (Calquence) in patients with relapsed or refractory CLL was based on a multicenter, randomized, open-label trial (ASCEND). The trial enrolled patients with relapsed or refractory CLL after at least one prior systemic therapy, while excluding those with transformed disease, prolymphocytic leukemia, or who had previous treatment with venetoclax, a Bruton tyrosine kinase inhibitor, or a phosphoinositide-3 kinase inhibitor. Interim analysis results indicate acalabrutinib (Calquence) significantly prolonged PFS when compared to rituximab combined with idelalisib or bendamustine.

Investigational or Not Medically Necessary Uses

I. Acalabrutinib (Calquence) has not been sufficiently evaluated outside of MCL and CLL/SLL. Limited evidence is available consisting of early phase studies evaluating use in other cancers; however, safety and efficacy have not been established in these conditions:
   A. Diffuse Large B-Cell Lymphoma
   B. Head and neck squamous cell carcinoma
   C. Ovarian cancer
   D. Non-small cell lung cancer (NSCLC)
   E. Severe Chronic Graft Versus Host Disease
   F. Waldenström's macroglobulinemia (WM)

References

1. Calquence [Prescribing Information]. Wilmington, DE: AstraZeneca; November 2019.
2. Wang M, Rule S, Zinzani PL, et al. Acalabrutinib in relapsed or refractory mantle cell lymphoma (ACE-LY-004): a single-arm, multicentre, phase 2 trial. Lancet. 2018;391(10121):659-667.

3. ClinicalTrials.gov. Elevate CLL TN: Study of Obinutuzumab + Chlorambucil, Acalabrutinib (ACP-196) + Obinutuzumab, and Acalabrutinib in Subjects With Previously Untreated CLL. NCT02475681
4. ClinicalTrials.gov. A Study of Acalabrutinib vs Investigator's Choice of Idelalisib Plus Rituximab or Bendamustine Plus Rituximab in R/R CLL. NCT02970318.
5. AstraZeneca (2019). ELEVATE-TN: Phase 3 Study of Acalabrutinib Combined with Obinutuzumab or Alone vs Obinutuzumab plus Chlorambucil in Patients with Treatment-Naïve Chronic Lymphocytic Leukemia [PowerPoint slides]. Retrieved from AstraZeneca.
6. AstraZeneca (2019). Acalabrutinib vs Rituximab plus Idelalisib or Bendamustine by Investigator's Choice in Relapsed/Refractory Chronic Lymphocytic Leukemia: Results from a Pre-Planed Interim Analysis of Phase 3 Ascend Study [PowerPoint slides]. Retrieved from AstraZeneca.

Policy Implementation/Update:

Date Created	January 2018
Date Effective	February 2018
Last Updated	December 2019
Last Reviewed	12/2019

Action and Summary of Changes	**Date**
Updated criteria to policy format. Addition of age requirement to ages 18 and older. Require member has not experienced disease progression while on a BTK inhibitor. Added new indication of CLL/SLL.	12/2019
Criteria created	01/2018