



# CALQUENCE®

(acalabrutinib) 100 mg capsules

## FOR FIRST-LINE OR R/R CLL/SLL<sup>1</sup>

CALQUENCE is a Bruton tyrosine kinase (BTK) inhibitor indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

### CLL patient population<sup>2</sup>

~20,720

ANNUAL  
INCIDENCE  
IN THE UNITED STATES\*

~70%  
AGED  
≥65 YEARS\*



DIAGNOSED  
NEARLY  
TWICE AS OFTEN IN  
MALES VS FEMALES\*

\*Based on SEER incidence rates from 2012 to 2016.

### Packaging and dosing<sup>1</sup>



NDC 60-count bottle:  
0310-0512-60

One 100-mg  
CAPSULE OF  
**CALQUENCE**  
IS TAKEN ORALLY  
APPROXIMATELY  
**every 12 hours**

### CALQUENCE efficacy<sup>1</sup>

- In patients with previously untreated CLL, CALQUENCE + obinutuzumab delivers a statistically significant improvement in PFS
  - 90% relative risk reduction in disease progression or death compared with obinutuzumab + chlorambucil (HR=0.10; 95% CI: 0.06, 0.17;  $P < 0.0001$ )
  - After a median follow-up of 28.3 months, median PFS was not yet reached with CALQUENCE + obinutuzumab vs 22.6 months with obinutuzumab + chlorambucil
- CALQUENCE monotherapy also demonstrated an 80% relative risk reduction in disease progression or death in previously untreated CLL (HR=0.20; 95% CI: 0.13, 0.30;  $P < 0.0001$ ) vs obinutuzumab + chlorambucil
- In R/R CLL, CALQUENCE demonstrated a 69% relative risk reduction in disease progression or death (HR=0.31; 95% CI: 0.20, 0.49;  $P < 0.0001$ ) vs IR or BR

### CALQUENCE has a proven safety profile<sup>1</sup>

- In patients with previously untreated CLL, adverse reactions led to dose reduction in 4% and 7% of patients in the CALQUENCE monotherapy and CALQUENCE + obinutuzumab arms, respectively. Adverse events led to discontinuation in 10% and 11% of patients, respectively
- In patients with R/R CLL, adverse reactions led to dose reductions in 4% of patients and discontinuation in 10% of patients
- The most common adverse reactions in patients with CLL ( $\geq 30\%$ ) of any grade were anemia, neutropenia, thrombocytopenia, headache, upper respiratory tract infection, and diarrhea

Please see accompanying full [Prescribing Information](#), including [Patient Information](#)

BR=bendamustine + rituximab; IR=idealisib + rituximab; NDC=National Drug Code; PFS=progression-free survival; R/R=relapsed/refractory; SEER=Surveillance, Epidemiology, and End Results Program.

### INDICATION AND USAGE

CALQUENCE is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

### IMPORTANT SAFETY INFORMATION ABOUT CALQUENCE® (acalabrutinib) capsules

#### Serious and Opportunistic Infections

Fatal and serious infections, including opportunistic infections, have occurred in patients with hematologic malignancies treated with CALQUENCE.

Serious or Grade 3 or higher infections (bacterial, viral, or fungal) occurred in 19% of 1029 patients exposed to CALQUENCE in clinical trials, most often due to respiratory tract infections (11% of all patients, including pneumonia in 6%). These infections predominantly occurred in the absence of Grade 3 or 4 neutropenia, with neutropenic infection reported in 1.9% of all patients. Opportunistic infections in recipients of CALQUENCE have included, but are not limited to, hepatitis B virus reactivation, fungal pneumonia, *Pneumocystis jirovecii* pneumonia, Epstein-Barr virus reactivation, cytomegalovirus, and progressive multifocal leukoencephalopathy (PML). Consider prophylaxis in patients who are at increased risk for opportunistic infections. Monitor patients for signs and symptoms of infection and treat promptly.

## IMPORTANT SAFETY INFORMATION ABOUT CALQUENCE® (acalabrutinib) capsules (cont'd)

### Hemorrhage

Fatal and serious hemorrhagic events have occurred in patients with hematologic malignancies treated with CALQUENCE. Major hemorrhage (serious or Grade 3 or higher bleeding or any central nervous system bleeding) occurred in 3.0% of patients, with fatal hemorrhage occurring in 0.1% of 1029 patients exposed to CALQUENCE in clinical trials. Bleeding events of any grade, excluding bruising and petechiae, occurred in 22% of patients.

Use of antithrombotic agents concomitantly with CALQUENCE may further increase the risk of hemorrhage. In clinical trials, major hemorrhage occurred in 2.7% of patients taking CALQUENCE without antithrombotic agents and 3.6% of patients taking CALQUENCE with antithrombotic agents. Consider the risks and benefits of antithrombotic agents when co-administered with CALQUENCE. Monitor patients for signs of bleeding. Consider the benefit-risk of withholding CALQUENCE for 3-7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

### Cytopenias

Grade 3 or 4 cytopenias, including neutropenia (23%), anemia (8%), thrombocytopenia (7%), and lymphopenia (7%), developed in patients with hematologic malignancies treated with CALQUENCE. Grade 4 neutropenia developed in 12% of patients. Monitor complete blood counts regularly during treatment. Interrupt treatment, reduce the dose, or discontinue treatment as warranted.

### Second Primary Malignancies

Second primary malignancies, including skin cancers and other solid tumors, occurred in 12% of 1029 patients exposed to CALQUENCE in clinical trials. The most frequent second primary malignancy was skin cancer, reported in 6% of patients. Monitor patients for skin cancers and advise protection from sun exposure.

### Atrial Fibrillation and Flutter

Grade 3 atrial fibrillation or flutter occurred in 1.1% of 1029 patients treated with CALQUENCE, with all grades of atrial fibrillation or flutter reported in 4.1% of all patients. The risk may be increased in patients with cardiac risk factors, hypertension, previous arrhythmias, and acute infection. Monitor for symptoms of arrhythmia (e.g., palpitations, dizziness, syncope, dyspnea) and manage as appropriate.

### ADVERSE REACTIONS

The most common adverse reactions (≥ 30%) of any grade in patients with CLL were anemia,\* neutropenia,\* thrombocytopenia,\* headache, upper respiratory tract infection, and diarrhea.

\*Treatment-emergent decreases (all grades) of hemoglobin, platelets, and neutrophils were based on laboratory measurements and adverse reactions.

In patients with previously untreated CLL exposed to CALQUENCE, fatal adverse reactions that occurred in the absence of disease progression and with onset within 30 days of the last study treatment were reported in 2% for each treatment arm, most often from infection. Serious adverse reactions were reported in 39% of patients in the CALQUENCE plus obinutuzumab arm and 32% in the CALQUENCE monotherapy arm, most often due to events of pneumonia (7% and 2.8%, respectively).

Adverse reactions led to CALQUENCE dose reduction in 7% and 4% of patients in the CALQUENCE plus obinutuzumab arm (N=178) and CALQUENCE monotherapy arm (N=179), respectively. Adverse events led to discontinuation in 11% and 10% of patients, respectively. Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 3.9% and 2.8% of patients in the CALQUENCE combination arm and monotherapy arm, respectively.

In patients with relapsed/refractory CLL exposed to CALQUENCE, serious adverse reactions occurred in 29% of patients. Serious adverse reactions in > 5% of patients who received CALQUENCE included lower respiratory tract infection (6%). Fatal adverse reactions within 30 days of the last dose of CALQUENCE occurred in 2.6% of patients, including from second primary malignancies and infection.

Adverse reactions led to CALQUENCE dose reduction in 3.9% of patients (N=154), dosage interruptions in 34% of patients, most often due to respiratory tract infections followed by neutropenia, and discontinuation in 10% of patients, most frequently due to second primary malignancies followed by infection. Increases in creatinine 1.5 to 3 times the upper limit of normal occurred in 1.3% of patients who received CALQUENCE.

### DRUG INTERACTIONS

**Strong CYP3A Inhibitors:** Avoid co-administration with a strong CYP3A inhibitor. If a strong CYP3A inhibitor will be used short-term, interrupt CALQUENCE.

**Moderate CYP3A Inhibitors:** When CALQUENCE is co-administered with a moderate CYP3A inhibitor, reduce CALQUENCE dose to 100 mg once daily.

**Strong CYP3A Inducers:** Avoid co-administration with a strong CYP3A inducer. If a strong CYP3A inducer cannot be avoided, increase the CALQUENCE dose to 200 mg approximately every 12 hours.

**Gastric Acid Reducing Agents:** If treatment with a gastric acid reducing agent is required, consider using an H2-receptor antagonist or an antacid. Take CALQUENCE 2 hours before taking an H2-receptor antagonist. Separate dosing with an antacid by at least 2 hours.

Avoid co-administration with proton pump inhibitors. Due to the long-lasting effect of proton pump inhibitors, separation of doses may not eliminate the interaction with CALQUENCE.

### SPECIFIC POPULATIONS

Based on findings in animals, CALQUENCE may cause fetal harm and dystocia when administered to a pregnant woman. There are no available data in pregnant women to inform the drug-associated risk. Advise pregnant women of the potential risk to a fetus.

Pregnancy testing is recommended for females of reproductive potential prior to initiating CALQUENCE therapy. Advise female patients of reproductive potential to use effective contraception during treatment with CALQUENCE and for at least 1 week following the last dose of CALQUENCE.

It is not known if CALQUENCE is present in human milk. Advise lactating women not to breastfeed while taking CALQUENCE and for at least 2 weeks after the final dose.

Avoid administration of CALQUENCE in patients with severe hepatic impairment. Dose modifications are not required for patients with mild or moderate hepatic impairment.

**Please see accompanying full Prescribing Information, including Patient Information**

**References:** 1. CALQUENCE [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2019. 2. SEER Cancer Stat Facts: leukemia - chronic lymphocytic leukemia (CLL). <https://seer.cancer.gov/statfacts/html/clyl.html>. Accessed August 15, 2019.