REVISED FORMULATION

CALQUENCE TABLETS

FREQUENTLY ASKED QUESTIONS

INDICATIONS AND USAGE

CALQUENCE is a Bruton tyrosine kinase (BTK) inhibitor 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.

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

Please see Important Safety Information throughout and full Prescribing Information, including Patient Information.

AstraZeneca

CALQUENCE®
acalabrutinib 100 mg tablets

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Please see Important Safety Information throughout and full Prescribing Information, including Patient Information.

CALQUENCE TABLETS | OVERVIEW

WHAT HAS CHANGED WITH CALQUENCE TABLETS?

ANSWER

CALQUENCE tablets can be taken with acid-reducing agents such as PPIs, antacids, or H2-receptor antagonists without any dosing restrictions or modifications. This means that there are no restrictions on taking CALQUENCE tablets concomitantly with any acid-reducing agent.[1,2]

Some common examples of PPIs are[3]:

- Nexium® (esomeprazole)
- Prevacid® (lansoprazole)
- Prilosec® (omeprazole)

Some common examples of antacids are[4]:

- Tums® (calcium carbonate)
- Rolaids® (calcium carbonate and magnesium hydroxide)

Some common examples of H2-receptor antagonists are[5]:

- Axid® (nizatidine)
- Pepcid®, Pepcid AC® (famotidine)
- Tagamet® (cimetidine)

PPI Coadministration

CALQUENCE can be taken with acid-reducing agents such as PPIs, antacids, or H2-receptor antagonists[1,2]

HOW IS PROTON PUMP INHIBITOR (PPI) COADMINISTRATION POSSIBLE?

ANSWER

Using PPIs can raise the gastric pH level of patients.[6] The CALQUENCE tablet formulation is an immediate-release film-coated tablet that has been shown to quickly and completely deliver the same amount of medicine at all physiological pH levels.[2]

IMPORTANT SAFETY INFORMATION ABOUT CALQUENCE® (acalabrutinib) tablets

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 jiroveci* 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.

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CALQUENCE TABLETS | OVERVIEW (cont'd)

ARE CALQUENCE CAPSULES STILL AVAILABLE FOR PRESCRIPTION AND USAGE?

ANSWER

No, CALQUENCE capsules are no longer available.

ARE THE EFFICACY AND SAFETY PROFILES OF CALQUENCE TABLETS EXPECTED TO BE THE SAME AS CALQUENCE CAPSULES?

ANSWER

Yes. Based on three Phase 1, open-label, single-dose, cross-over studies conducted in healthy subjects to establish bioequivalence, CALQUENCE tablets are expected to have the same efficacy and safety as CALQUENCE capsules.[2]

Same Efficacy and Safety Expected

The tablet formulation has been proven to be bioequivalent to capsules[2]

IMPORTANT SAFETY INFORMATION ABOUT CALQUENCE® (acalabrutinib) tablets (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.

Please see Important Safety Information throughout and full Prescribing Information, including Patient Information.

CALQUENCE TABLETS | DOSING

HOW SHOULD CALQUENCE TABLETS BE TAKEN?

ANSWER

The dosing regimen of CALQUENCE tablets is the same as CALQUENCE capsules[1,7]:

SAME STRENGTH, SAME STRAIGHTFORWARD DOSING REGIMEN[1]

Not actual tablet size.

One 100-mg tablet of CALQUENCE is taken orally twice daily

Take approximately every 12 hours until disease progression or unacceptable toxicity

Tablet should be swallowed whole with water, without being chewed, crushed, dissolved, or cut

CALQUENCE can be taken with or without food

ARE THERE ANY CHANGES TO THE DOSING SCHEDULE?

ANSWER

There are no changes to the dosing schedule with CALQUENCE tablets. Patients should take one CALQUENCE 100-mg tablet approximately every 12 hours until disease progression or unacceptable toxicity.[1]

CAN CALQUENCE TABLETS BE CRUSHED, DISSOLVED, DIVIDED, OR ALTERED IN ANY WAY?

ANSWER

CALQUENCE tablets should be swallowed whole with water, without being chewed, crushed, dissolved, or cut.[1]

CAN CALQUENCE TABLETS BE DOSED AS A MONOTHERAPY OR IN COMBINATION WITH OBINUTUZUMAB?

ANSWER

Like CALQUENCE capsules, CALQUENCE tablets can be dosed as a monotherapy in patients with CLL/SLL or relapsed/refractory MCL. CALQUENCE tablets can also be dosed in combination with obinutuzumab in the same regimen, in patients with previously untreated CLL or SLL.[1,7]

CLL=chronic lymphocytic leukemia; MCL=mantle cell lymphoma; SLL=small lymphocytic lymphoma.

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

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.

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CALQUENCE TABLETS | DOSAGE MODIFICATIONS

HOW HAVE DOSAGE MODIFICATIONS CHANGED WITH CALQUENCE TABLETS?

ANSWER

Acid-Reducing Agents

There are no dosage modifications needed when taking CALQUENCE tablets with acid-reducing agents such as PPIs, antacids, or H2-receptor antagonists.[1,2]

CYP3A Inhibitors or Inducers

Dosage modifications for taking CALQUENCE tablets with CYP3A inhibitors or inducers remain the same.[1]
Please see Important Safety Information on page 9 and consult the Prescribing Information (PI) for recommended dosage modifications.

Grade ≥3 Adverse Reactions

Dosage modifications for adverse reactions of Grade ≥3 remain the same with CALQUENCE tablets.[1]
Please consult the PI for recommended dosage modifications.

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

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.

CALQUENCE TABLETS | ADDITIONAL QUESTIONS

IS THERE A DIFFERENCE IN COST AND/OR INSURANCE COVERAGE WITH TABLETS VERSUS CAPSULES?

ANSWER

No. There is no anticipated change in cost or insurance coverage with CALQUENCE 100 mg tablets.

ARE NEW PRESCRIPTIONS REQUIRED FOR THE CALQUENCE TABLETS?

ANSWER

Yes. New prescriptions need to be written for CALQUENCE 100-mg tablets.

ARE REAUTHORIZATIONS REQUIRED FOR CALQUENCE TABLETS?

ANSWER

No. CALQUENCE tablets do not require reauthorization access.

WHAT ARE THE PHYSICAL DIFFERENCES BETWEEN CALQUENCE CAPSULES AND TABLETS?

ANSWER

CALQUENCE tablets are smaller in size when compared to CALQUENCE capsules. Additionally, tablets have a film coating to improve swallowing ability.[2]

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

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 (eg, palpitations, dizziness, syncope, dyspnea) and manage as appropriate.

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INDICATIONS AND IMPORTANT SAFETY INFORMATION

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Second Primary Malignancies

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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 (eg, palpitations, dizziness, syncope, dyspnea) and manage as appropriate.

ADVERSE REACTIONS

The most common adverse reactions (≥20%) of any grade in patients with relapsed or refractory MCL were anemia,* thrombocytopenia,* headache (39%), neutropenia,* diarrhea (31%), fatigue (28%), myalgia (21%), and bruising (21%). The most common Grade ≥3 non-hematological adverse reaction (reported in at least 2% of patients) was diarrhea (3.2%).

*Treatment-emergent decreases (all grades) of hemoglobin (46%), platelets (44%), and neutrophils (36%) were based on laboratory measurements and adverse reactions.

INDICATIONS AND IMPORTANT SAFETY INFORMATION (cont'd)

ADVERSE REACTIONS (cont'd)

Dose reductions or discontinuations due to any adverse reaction were reported in 1.6% and 6.5% of patients, respectively. Increases in creatinine to 1.5 to 3 times the upper limit of normal (ULN) occurred in 4.8% of patients.

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 to 1.5 to 3 times ULN 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), dose 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 to 1.5 to 3 times ULN occurred in 1.3% of patients who received CALQUENCE.

DRUG INTERACTIONS

Strong CYP3A Inhibitors: Avoid co-administration of CALQUENCE with a strong CYP3A inhibitor. If these inhibitors will be used short-term, interrupt CALQUENCE. After discontinuation of strong CYP3A inhibitor for at least 24 hours, resume previous dosage of CALQUENCE.

Moderate CYP3A Inhibitors: Reduce the dosage of CALQUENCE to 100 mg once daily when co-administered with a moderate CYP3A inhibitor.

Strong CYP3A Inducers: Avoid co-administration of CALQUENCE with a strong CYP3A inducer. If co-administration is unavoidable, increase the dosage of CALQUENCE to 200 mg approximately every 12 hours.

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 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 2 weeks after the last dose.

Avoid use of CALQUENCE in patients with severe hepatic impairment (Child-Pugh class C). No dosage adjustment of CALQUENCE is recommended in patients with mild (Child-Pugh class A) or moderate (Child-Pugh class B) hepatic impairment.

Please see full Prescribing Information, including Patient Information.

CALQUENCE®
acalabrutinib 100 mg tablets

References: 1. CALQUENCE® (acalabrutinib) tablets [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2022. **2.** Sharma S, Pepin X, Burri H, et al. New acalabrutinib formulation enables co-administration with proton pump inhibitors and dosing in patients unable to swallow capsules (ELEVATE-PLUS). *Blood*. 2021; 138(Suppl 1):4365. doi.org/10.1181/blood-2021-146610 **3.** Proton pump inhibitors. US National Library of Medicine. Updated November 23, 2020. Accessed November 30, 2020. https://medlineplus.gov/ency/patientinstructions/000381.htm **4.** Calcium Carbonate. US National Library of Medicine. Updated February 7, 2022. Accessed February 24, 2022. https://medlineplus.gov/druginfo/meds/a601032.html **5.** H2 blockers. US National Library of Medicine. Updated February 18, 2022. Accessed February 24, 2022. https://medlineplus.gov/ency/patientinstructions/000382.htm **6.** Freedberg DE, Lebwohl B, Abrams JA. The impact of proton pump inhibitors on the human gastrointestinal microbiome. *Clin Lab Med*. 2014;34(4):771-785. doi.org/10.1016/j.cll.2014.08.008 **7.** CALQUENCE® (acalabrutinib) capsules [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2022. **8.** Data on File, REF-143914. AstraZeneca Pharmaceuticals LP.

Please read Important Safety Information throughout and full Prescribing Information for CALQUENCE, including Patient Information, or scan here.

CALQUENCE® acalabrutinib 100 mg tablets