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

## 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).

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**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.

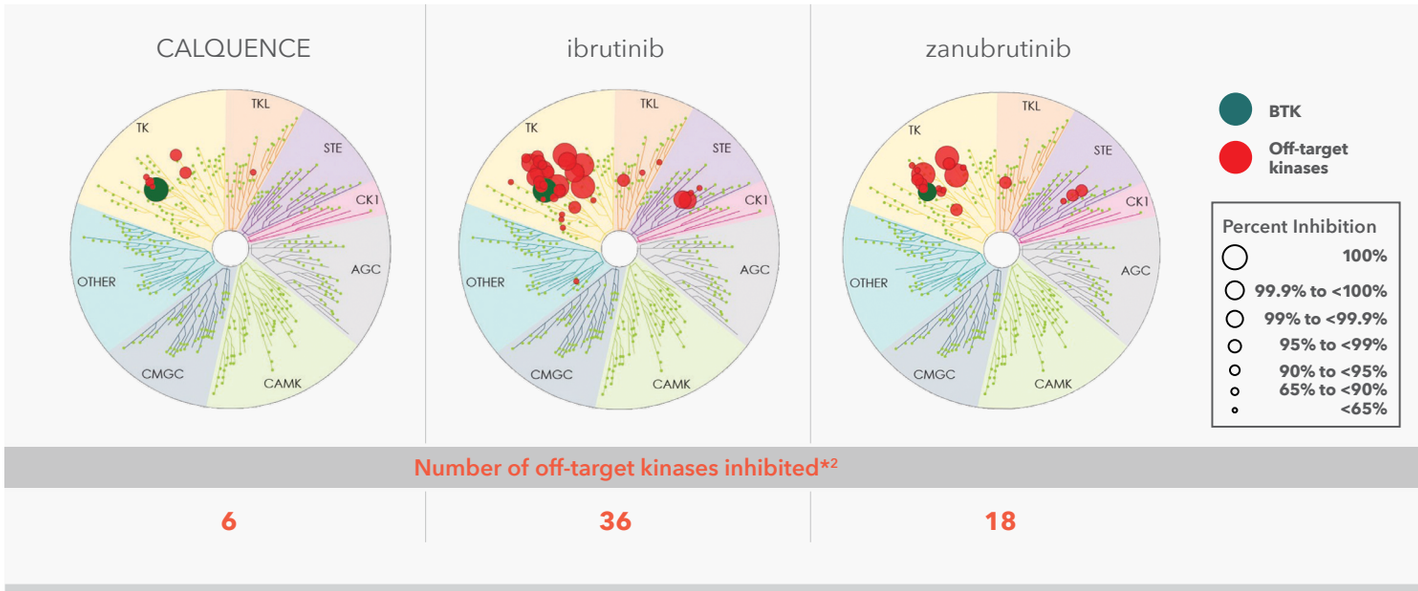
**Please see Important Safety Information throughout and on pages 8-9, and accompanying full Prescribing Information, including Patient Information.**

CALQUENCE®
(acalabrutinib) 100 mg capsules

# CALQUENCE: A NEXT-GENERATION BTKi WITH HIGH SELECTIVITY AND LIMITED OFF-TARGET ACTIVITY[1-3]

## CALQUENCE demonstrated inhibition across fewer off-target kinases[2,4]

***CALQUENCE selectively targets BTK, with limited inhibition of off-target kinases, including EGFR, ITK, and TEC[2,4]***




| Number of off-target kinases inhibited*[2] | | |
|---|---|---|
| 6 | 36 | 18 |

*Number of kinases (excluding BTK) inhibited >65% at a single dose (1 µM), using KINOMEscan™.[2]

Results are based on an active site competitive binding assay implicating kinase inhibition.[2]

In the TREE*spot*™ interaction maps developed by KINOMEscan™, some circles are overlapping, and therefore, counting may be difficult.[2]
Eight additional non-mutant human kinases were added to the panel used for testing zanubrutinib (conducted in 2017), compared to the panel used for testing the other BTK inhibitors (conducted in 2014). Zanubrutinib did not inhibit any of these kinases by ≥65%.[2]

- CALQUENCE selectively targets BTK[2,4]
- CALQUENCE is a more potent inhibitor of BTK than of any other kinase[4]
- CALQUENCE inhibits fewer off-target kinases, such as TEC, EGFR, and ITK[4]

Profiles of CALQUENCE, ibrutinib, and zanubrutinib in a competitive binding assay of more than 450 human kinases and disease-relevant mutants. Compounds were tested at a single concentration of 1 µM. The degree of inhibition vs untreated control is represented by red circle size.[2]

The clinical relevance of these pharmacologic data has not been determined. There are no head-to-head trials between CALQUENCE, ibrutinib, or zanubrutinib comparing safety or efficacy.

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

### 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.

# CONTINUOUS BTK INHIBITION THROUGH DOSING APPROXIMATELY EVERY 12 HOURS[5,6]

## Prescribe one straightforward dosing regimen

- CALQUENCE maintained a median steady-state BTK occupancy of ≥95% in peripheral blood over 12 hours, inactivating BTK throughout the recommended dosing interval[6]
- Durable and near-complete inhibition of BTK with CALQUENCE is achieved across key disease sites, including blood, lymph nodes, and bone marrow, with twice-daily dosing[†5]

Not actual pill size.

One 100-mg capsule of CALQUENCE is taken orally twice daily[6]


Take approximately every 12 hours[6]

CALQUENCE can be taken with or without food[6]

Capsule should be swallowed whole with water, and should not be opened, broken, or chewed[6]

If a dose is missed by more than 3 hours, it should be skipped and the next dose should be taken at its regularly scheduled time. Extra capsules should not be taken to make up for a missed dose.[6]

[†]BTK resynthesis rates are comparable between blood and lymph nodes in CLL.[5]
BTKi=Bruton tyrosine kinase inhibitor; EGFR=epidermal growth factor receptor; ITK=IL2-inducible T-cell kinase; R/R=relapsed/refractory; TEC=tyrosine kinase expressed in hepatocellular carcinoma.

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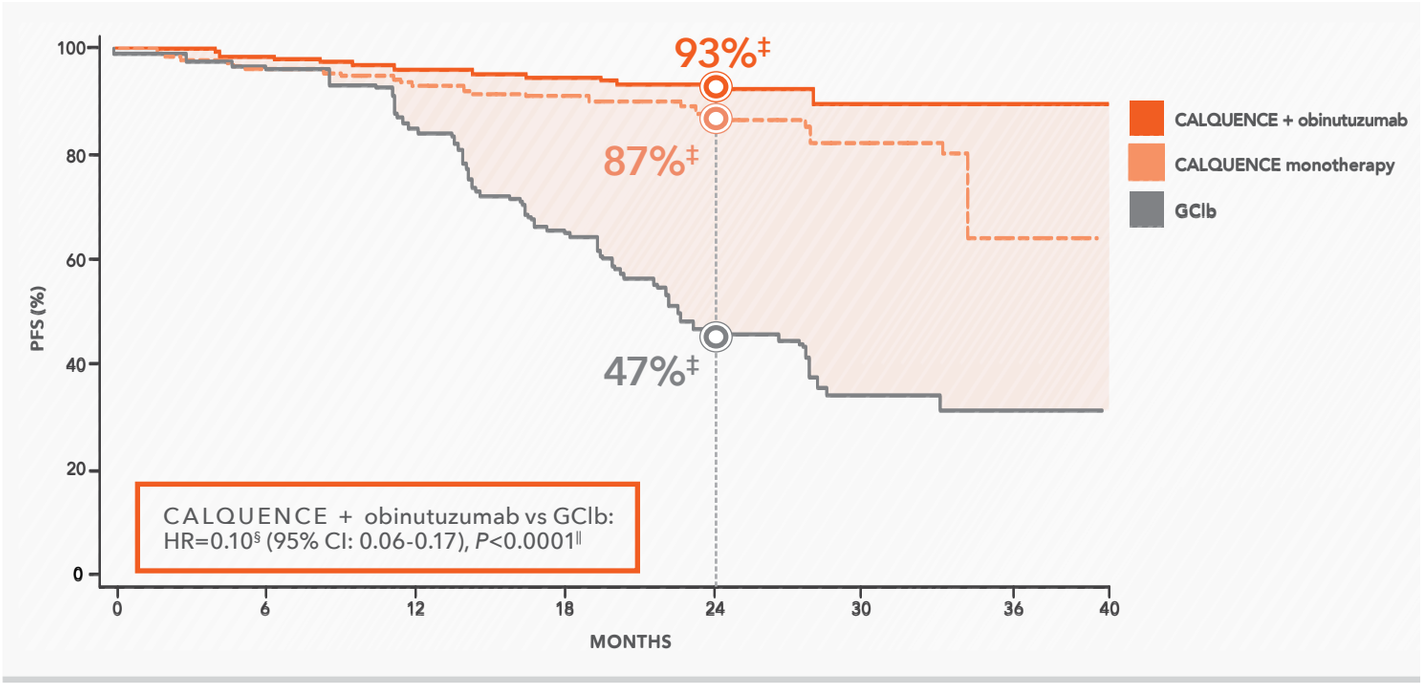
CALQUENCE® (acalabrutinib) 100 mg capsules

# CALQUENCE: A BTKi THAT DELIVERED UNPRECEDENTED PFS

## 90% risk reduction in disease progression or death with CALQUENCE + obinutuzumab vs GClb[6]

At median 28.3-month follow-up (range: 0.0 to 40.8 months), median PFS was not reached with CALQUENCE + obinutuzumab vs 22.6 months (95% CI: 20-28) with GClb*[6]

### *IRC-ASSESSED PROGRESSION-FREE SURVIVAL*†[6,7]




## STRONG EFFICACY WITH CALQUENCE + OBINUTUZUMAB AND CALQUENCE MONOTHERAPY[6]

- CALQUENCE monotherapy vs GClb: 80% risk reduction in disease progression or death (HR=0.20§ [95% CI: 0.13-0.30], *P*<0.0001‖)
- Median PFS was not reached with CALQUENCE monotherapy (95% CI: 34-NE) vs 22.6 months (95% CI: 20-28) with GClb

### Study Design

ELEVATE-TN was a Phase 3, open-label, randomized, multicenter trial in patients with previously untreated CLL (N=535). Patients were randomized 1:1:1 to receive either CALQUENCE + obinutuzumab (n=179), CALQUENCE monotherapy (n=179), or GClb (n=177). Patients in the CALQUENCE arms received 100 mg approximately every 12 hours until disease progression or unacceptable toxicity. The primary comparison was PFS between the CALQUENCE + obinutuzumab and GClb arms. PFS for CALQUENCE monotherapy vs GClb was a secondary endpoint in the study.[6,7]

*Per 2008 International Workshop on CLL criteria.[6]

†At the time of analysis, the number of events in each arm was 14 (8%) for CALQUENCE + obinutuzumab, 26 (15%) for CALQUENCE monotherapy, and 93 (53%) for GClb.[6]

‡Estimated 24-month PFS: CALQUENCE + obinutuzumab 93% (95% CI: 87-96); CALQUENCE monotherapy 87% (95% CI: 81-92); and GClb 47% (95% CI: 39-55).[7]

§Based on a stratified Cox proportional-hazards model, both hazard ratios were compared with the GClb arm.[6]

‖Based on a stratified log-rank test, with an alpha level of 0.012 derived from alpha spending function by the O'Brien-Fleming method.[6]

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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 (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.

# SAFETY AND TOLERABILITY CONSISTENT WITH THE ESTABLISHED PROFILE OF CALQUENCE

## *COMMON ADVERSE REACTIONS (≥15%, ANY GRADE) WITH CALQUENCE IN ELEVATE-TN*[*6]

| ADVERSE REACTION | CALQUENCE + obinutuzumab (n=178) | | CALQUENCE monotherapy (n=179) | | GClb (n=169) | |
|---|---|---|---|---|---|---|
| | All Grades (%) | Grade ≥3 (%) | All Grades (%) | Grade ≥3 (%) | All Grades (%) | Grade ≥3 (%) |
| Infection[†] | 69 | 22[‡] | 65 | 14[‡] | 46 | 13[‡] |
| Upper respiratory tract infection[†] | 39 | 2.8 | 35 | 0 | 17 | 1.2 |
| Lower respiratory tract infection[†] | 24 | 8 | 18 | 4.5 | 7 | 1.8 |
| Urinary tract infection | 15 | 1.7 | 15 | 2.8 | 5 | 0.6 |
| Neutropenia[†] | 53 | 37 | 23 | 13 | 78 | 50 |
| Anemia[†] | 52 | 12 | 53 | 10 | 54 | 14 |
| Thrombocytopenia[†] | 51 | 12 | 32 | 3.4 | 61 | 16 |
| Lymphocytosis[†] | 12 | 11 | 16 | 15 | 0.6 | 0.6 |
| Headache | 40 | 1.1 | 39 | 1.1 | 12 | 0 |
| Dizziness | 20 | 0 | 12 | 0 | 7 | 0 |
| Diarrhea | 39 | 4.5 | 35 | 0.6 | 21 | 1.8 |
| Nausea | 20 | 0 | 22 | 0 | 31 | 0 |
| Musculoskeletal pain[†] | 37 | 2.2 | 32 | 1.1 | 16 | 2.4 |
| Arthralgia | 22 | 1.1 | 16 | 0.6 | 4.7 | 1.2 |
| Fatigue[†] | 34 | 2.2 | 23 | 1.1 | 24 | 1.2 |
| Bruising[†] | 31 | 0 | 21 | 0 | 5 | 0 |
| Rash[†] | 26 | 2.2 | 25 | 0.6 | 9 | 0.6 |
| Hemorrhage[†] | 20 | 1.7 | 20 | 1.7 | 6 | 0 |

Other clinically relevant adverse reactions (<15%, any grade) in recipients of CALQUENCE (CALQUENCE + obinutuzumab and as monotherapy) included neoplasms (second primary malignancy [10%], including non-melanoma skin cancer [5%]); infection (herpesvirus infection [6%]); and cardiac disorders (atrial fibrillation or flutter [3.6%], hypertension [5%]).[6]

Select non-hematologic laboratory abnormalities (≥15%, any grade) that were new or worsening from baseline in patients receiving CALQUENCE included increases in uric acid, alanine aminotransferase, aspartate aminotransferase, and bilirubin.[6]

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 + obinutuzumab and CALQUENCE monotherapy arms, respectively.[6]

## Low rates of select cardiac adverse events[7]

### ATRIAL FIBRILLATION

| CALQUENCE + obinutuzumab | | CALQUENCE monotherapy |
|---|---|---|
| 3% | All grades | 4% |
| 1% | Grade ≥3 | 0% |

+ No ventricular tachyarrhythmias reported[7]

### HYPERTENSION

| CALQUENCE + obinutuzumab | | CALQUENCE monotherapy |
|---|---|---|
| 7% | All grades | 5% |
| 3% | Grade ≥3 | 2% |

+ No Grade 4/5 atrial fibrillation or hypertension reported[8]

*The median duration of exposure to CALQUENCE in the CALQUENCE + obinutuzumab and CALQUENCE monotherapy arms was 27.7 months (range: 0.3 to 40 months).[6]

[†]Includes multiple adverse drug reaction terms (see full Prescribing Information).[6]

[‡]Includes 3 fatal cases in the CALQUENCE + obinutuzumab arm, 3 fatal cases in the CALQUENCE monotherapy arm, and 1 fatal case in the GClb arm.[6]

CI=confidence interval; GClb=obinutuzumab + chlorambucil; HR=hazard ratio; IRC=Independent Review Committee; NE=not estimable; PFS=progression-free survival.

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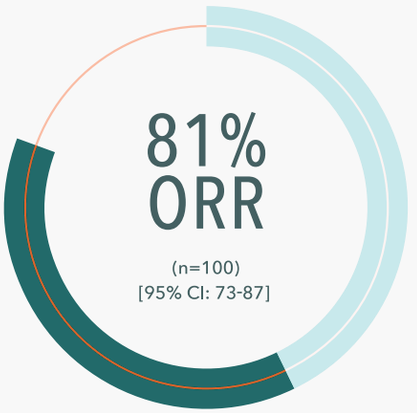
CALQUENCE® (acalabrutinib) 100 mg capsules

# CALQUENCE: A BTKi THAT DEMONSTRATED STRONG AND DURABLE EFFICACY OVER TIME

## In the initial data analysis, 8 out of 10 patients achieved a response*†‡[6,9]

- 80% ORR (n=99) [95% CI: 72-87]
  - 40% CR (n=49) [95% CI: 31-49]
  - 40% PR (n=50) [95% CI: 32-50]

### *Consistent response rates at 24-month update analysis (N=124)*[§10]




**43% CR**
(n=53)
[95% CI: 34-52]

**38% PR**
(n=47)
[95% CI: 29-47]

- **Of those patients who responded to CALQUENCE, 53% (53/100) achieved a complete response[10]**

## CALQUENCE delivered meaningful measures of response

**Median DoR of 26 months (more than 2 years)[§‖10]**

**Median PFS of 20 months (more than 1.5 years)[§10]**
[95% CI: 16.5-27.7]

- Median follow-up was 26 months (range: 0.3 to 35.1 months)[10]
- At the time of PFS analysis, 66 events (53.2%) had occurred[11]

**LY-004 trial:** an international, Phase 2, open-label, multicenter trial of 124 patients (≥18 years) with MCL who had received ≥1 prior therapy. Patients received CALQUENCE 100 mg approximately every 12 hours until disease progression or unacceptable toxicity. The primary endpoint was ORR; secondary endpoints included DoR, PFS, and OS.[9]

**The initial data analysis** was based on efficacy and safety endpoints that occurred from March 12, 2015, through approximately 14 months after the last subject was enrolled.[9]

**The 24-month update analysis** was based on the cumulative efficacy and safety endpoints that occurred from March 12, 2015, until February 12, 2018.[9,10]

*Independent Review Committee–assessed per 2014 Lugano Classification.[6]
†Median follow-up of 15.2 months.[6]
‡Investigator-assessed response rates were ORR: 81%; CR: 40%; PR: 41%.[6]
§Investigator-assessed per 2014 Lugano Classification.[9,10]
‖DoR was measured in the 100 subjects who achieved a CR or PR.[10]

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### ADVERSE REACTIONS (cont'd)

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.

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

# LONG-TERM SAFETY PROFILE CONSISTENT WITH INITIAL ANALYSIS

## Safety profile from the initial data analysis*[6]

- Most common adverse drug reactions (≥20%) were anemia, thrombocytopenia, headache, neutropenia, diarrhea, fatigue, myalgia, and bruising
- Few patients had dose reductions (1.6%) or discontinued treatment (6.5%) due to adverse events (N=124)

## Safety profile from 24-month update analysis†[10]

- Most common treatment-emergent adverse events (≥20%) were headache, diarrhea, fatigue, cough, and myalgia
- Low rates of dose reduction (2%) and discontinuation (8%) due to AEs (N=124)
- The most common events, headache and diarrhea, were mostly low grade, with improvement over time

### *Treatment-emergent AEs reported in ≥10% of all patients (N=124)*[10]

| ADVERSE EVENT, n (%)‡ | ANY GRADE | GRADE 3 | GRADE 4 |
|---|---|---|---|
| Headache | 47 (38) | 2 (2) | 0 |
| Diarrhea | 45 (36) | 4 (3) | 0 |
| Fatigue | 35 (28) | 2 (2) | 0 |
| Cough | 27 (22) | 0 | 0 |
| Myalgia | 26 (21) | 2 (2) | 0 |
| Nausea | 24 (19) | 2 (2) | 0 |
| Asthenia | 21 (17) | 2 (2) | 0 |
| Pyrexia | 20 (16) | 0 | 0 |
| Constipation | 19 (15) | 0 | 0 |
| Vomiting | 18 (15) | 3 (2) | 0 |
| Rash | 17 (14) | 2 (2) | 0 |
| Anemia | 16 (13) | 12 (10) | 1 (1) |
| Contusion | 16 (13) | 0 | 0 |
| Dizziness | 15 (12) | 0 | 0 |
| Sinusitis | 15 (12) | 0 | 0 |
| Dyspnea | 13 (10) | 2 (2) | 1 (1) |
| Neutropenia§ | 13 (10) | 6 (5) | 7 (6) |
| Upper respiratory tract infection | 13 (10) | 0 | 0 |

Grade 5 events included pulmonary embolism, aortic stenosis, myelodysplastic syndrome, pneumonia, suicide, and non-small cell lung cancer.[10]

## Treatment-emergent AEs of clinical interest (N=124)‖¶[10]:

- AEs (all grades/Grade 3 or 4) reported in patients included infections (61.3%/15%), hemorrhage (33.1%/2.4%), leukopenia (13.7%/13.7%), anemia (12.9%/10.5%), cardiac events (10%/3%), second primary malignancies# (8.1%/2.4%), thrombocytopenia (6.5%/4.8%), hepatic events (4.0%/1.6%), and interstitial lung disease/pneumonitis (2.4%/0.8%)

## Low rates of select cardiac adverse events[9,10]

**ATRIAL FIBRILLATION**

**0%** — Initial analysis

**0%**** — 24-month update analysis

**HYPERTENSION**

**3%††** — Initial analysis

**3%‡‡** — 24-month update analysis

*Median duration of therapy was 16.6 months (range: 0.1 to 26.6 months).[6]

†Median duration of therapy was 17.3 months (range: 0.1 to 35.1 months).[10]

‡No Grade 5 events were reported for these adverse events.[10]

§One case of Grade 3 febrile leukopenia occurred but is not included in the total shown here since it was reported as a separate preferred term.[10]

‖Events of clinical interest were coded using the MedDRA Version 20.1.[11]

¶Events of clinical interest were identified based on nonclinical findings, emerging data from clinical studies relating to CALQUENCE, and pharmacological effects of an approved BTKi.[11]

#There was one Grade 5 adverse event of clinical interest (non-small cell lung cancer) reported in the 24-month update.[11]

**One patient was initially assessed as experiencing an AE of atrial fibrillation, but the condition was later determined to be preexisting and not treatment-related.[10]

††Four patients had hypertension events, with one Grade 3 event.[10]

‡‡There were no NEW cases of hypertension in the 24-month update analysis.[10]

AE=adverse event; CR=complete response; DoR=duration of response; ORR=overall response rate; OS=overall survival; PR=partial response.

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CALQUENCE® (acalabrutinib) 100 mg capsules

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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).

### 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 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.

#### 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.

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#### 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 (≥ 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.

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

*You are encouraged to report negative side effects of AstraZeneca prescription drugs by calling 1-800-236-9933. If you prefer to report these to the FDA, either visit www.FDA.gov/medwatch or call 1-800-FDA-1088.*

**References: 1.** Bond DA, Woyach JA. Targeting BTK in CLL: beyond ibrutinib. *Curr Hematol Malig Rep*. 2019;14(3):197-205. **2.** Data on File, REF-92495. AstraZeneca Pharmaceuticals LP. **3.** Tam CS, LeBlond V, Novotny W, et al. A head-to-head phase III study comparing zanubrutinib versus ibrutinib in patients with Waldenström macroglobulinemia. *Future Oncol*. 2018;14(22):2229-2237. **4.** Byrd JC, Harrington B, O'Brien S, et al. Acalabrutinib (ACP-196) in relapsed chronic lymphocytic leukemia. *N Engl J Med.* 2016;374(4):323-332. **5.** Sun C, Nierman P, Kendall EK, et al. Clinical and biological implications of target occupancy in CLL treated with the BTK inhibitor acalabrutinib. *Blood*. 2020;136(1):93-105. **6.** CALQUENCE [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2019. **7.** Sharman JP, Egyed M, Jurczak W, et al. Acalabrutinib with or without obinutuzumab versus chlorambucil and obinutuzumab for treatment-naive chronic lymphocytic leukaemia (ELEVATE TN): a randomised, controlled, phase 3 trial [published correction appears in *Lancet.* 2020;395(10238):1694]. *Lancet*. 2020;395(10232):1278-1291. **8.** Data on File, REF-78409. AstraZeneca Pharmaceuticals LP. **9.** 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. **10.** Wang M, Rule S, Zinzani PL, et al. Durable response with single-agent acalabrutinib in patients with relapsed or refractory mantle cell lymphoma. *Leukemia*. 2019;33(11):2762-2766. **11.** Data on File, REF-43179. AstraZeneca Pharmaceuticals, LP. **12.** Data on File, US-43772. AstraZeneca Pharmaceuticals LP.

# NOTES

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CLL MCL

# CALQUENCE — COMPREHENSIVE ASSISTANCE

>80% of commercially insured patients prescribed CALQUENCE pay **as little as** $0 out of pocket.[12]

## CALQUENCE PATIENT SAVINGS PROGRAM

**for eligible commercially insured patients**

**MOST ELIGIBLE PATIENTS WILL PAY AS LITTLE AS $0 PER MONTH**

- Patients may have access to up to $26,000 per year to assist with CALQUENCE out-of-pocket costs
- There are no income requirements to participate in the program

Subject to eligibility. Restrictions apply.

For additional information, please visit **astrazenecaspecialtysavings.com**.

## HELPING PATIENTS ACCESS THE CARE THEY NEED

AstraZeneca Access 360™

The AstraZeneca Access 360™ program provides personal support to help streamline access and reimbursement for CALQUENCE.

To learn more about the Access 360 program, please call **1-844-ASK-A360 (1-844-275-2360)**, Monday–Friday, 8 AM–8 PM ET, or visit **www.MyAccess360.com**

## FIND OUT MORE ABOUT WHAT CALQUENCE CAN DO FOR YOUR PATIENTS WITH CLL/SLL OR R/R MCL AT CALQUENCEHCP.COM

**Please see Important Safety Information throughout and on pages 8-9, and accompanying full Prescribing Information, including Patient Information.**

AstraZeneca



CALQUENCE® (acalabrutinib) 100 mg capsules