



# PATIENT MANAGEMENT

This guide provides information that may help you manage potential adverse reactions (ARs) and side effects

Information for BRUKINSA is based on data from the pooled safety population across the largest range of B-cell malignancies (N=1729)\*<sup>1-4</sup>

\*Includes chronic lymphocytic leukemia, Waldenström's macroglobulinemia, mantle cell lymphoma, follicular lymphoma, marginal zone lymphoma, hairy cell leukemia, diffuse large B-cell lymphoma, and Richter's transformation.<sup>1</sup>

## INDICATIONS

BRUKINSA is a kinase inhibitor indicated for the treatment of adult patients with:

- Chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)
- Waldenström's macroglobulinemia (WM)
- Mantle cell lymphoma (MCL) who have received at least one prior therapy
- Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen
- Relapsed or refractory follicular lymphoma (FL), in combination with obinutuzumab, after two or more lines of systemic therapy

The MCL, MZL and FL indications are approved under accelerated approval based on overall response rate and durability of response. Continued approval for these indications may be contingent upon verification and description of clinical benefit in confirmatory trials.

**Please see Important Safety Information throughout and accompanying full Prescribing Information.**

# MANAGEMENT OF COMMON ARs ASSOCIATED WITH BRUKINSA

In the pooled safety population of 1729 patients, the most common ARs ( $\geq 30\%$ ) associated with BRUKINSA, including laboratory abnormalities, were neutropenia (51%), thrombocytopenia (41%), upper respiratory tract infection (38%), hemorrhage (32%), and musculoskeletal pain (31%).<sup>2</sup>

Below are general recommendations for managing common ARs associated with BRUKINSA.

| RECOMMENDATIONS FOR COMMON ARs <sup>5</sup> |  |
|---|--|
| Neutropenia                                 | Recommendations include antibiotics to prevent infections and white blood cell growth factors. Practicing good personal hygiene may lower the patient's risk of infection, including regularly washing hands and avoiding contact with people who are sick.  |
| Thrombocytopenia                            | Recommendations include regular blood tests to monitor platelet counts, medications that may prevent low platelet counts, and transfusions for the temporary treatment of very low platelet counts. Additional prevention techniques include avoiding situations that could cause bleeding. Self-care methods such as using an extra soft toothbrush and brushing gently, shaving with an electric razor, avoiding activities that may cause injury, avoiding burns while cooking, and using a nail file instead of nail clippers may help to prevent bleeding when platelet counts are low. |

## IMPORTANT SAFETY INFORMATION WARNINGS AND PRECAUTIONS

### Hemorrhage

Fatal and serious hemorrhage has occurred in patients with hematological malignancies treated with BRUKINSA. Grade 3 or higher hemorrhage including intracranial and gastrointestinal hemorrhage, hematuria, and hemothorax was reported in 3.8% of patients treated with BRUKINSA in clinical trials, with fatalities occurring in 0.2% of patients. Bleeding of any grade, excluding purpura and petechiae, occurred in 32% of patients.

Bleeding has occurred in patients with and without concomitant antiplatelet or anticoagulation therapy. Coadministration of BRUKINSA with antiplatelet or anticoagulant medications may further increase the risk of hemorrhage.

Monitor for signs and symptoms of bleeding. Discontinue BRUKINSA if intracranial hemorrhage of any grade occurs. Consider the benefit-risk of withholding BRUKINSA for 3-7 days before and after surgery depending upon the type of surgery and the risk of bleeding.

| RECOMMENDATIONS FOR COMMON ARs (continued) <sup>2,5</sup> |   |
|---|---|
| Upper Respiratory Tract Infection                         | Recommendations include monitoring for signs of infection, such as fevers, chills, increased heart rate, breathing issues, and coughing. Blood tests, x-rays, and sputum sampling can be used to confirm the presence of infection. Anti-infectives, including antibiotics and antivirals, are the standard treatment protocol. |
| Hemorrhage  | Recommendations include monitoring for signs of bleeding, bandaging of wounds, and discontinuation of treatment.  |
| Musculoskeletal Pain (Arthralgia, Myalgia)                | Recommendations include using over-the-counter pain medicines such as ibuprofen, naproxen, or acetaminophen, or other medications such as muscle relaxers and corticosteroids. Some self-care and support methods to treat musculoskeletal pain include massage, physical therapy, exercise, acupuncture, and heat and cold.    |

## IMPORTANT SAFETY INFORMATION (continued) WARNINGS AND PRECAUTIONS (continued)

### Infections

Fatal and serious infections (including bacterial, viral, or fungal infections) and opportunistic infections have occurred in patients with hematological malignancies treated with BRUKINSA. Grade 3 or higher infections occurred in 26% of patients, most commonly pneumonia (7.9%), with fatal infections occurring in 3.2% of patients. Infections due to hepatitis B virus (HBV) reactivation have occurred.

Consider prophylaxis for herpes simplex virus, *pneumocystis jirovecii* pneumonia, and other infections according to standard of care in patients who are at increased risk for infections. Monitor and evaluate patients for fever or other signs and symptoms of infection and treat appropriately.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.



## AEs OF SPECIAL INTEREST

| ADVERSE EVENTS <sup>1</sup> | BRUKINSA<br>All Grades (%)         | BRUKINSA<br>Grade $\geq 3$ (%) |
|-----------------------------|------------------------------------|--------------------------------|
|                             | Pooled Safety Population (N=1729)* |                                |
| Rash                        | 25                                 | 0.6                            |
| Diarrhea                    | 20                                 | 2                              |
| Fatigue                     | 18                                 | 1                              |
| Headache                    | 11                                 | 0.3                            |
| Arthralgia                  | 14                                 | 0.6                            |
| Myalgia                     | 4                                  | 0.3                            |
| Afib/flutter                | 4                                  | 2                              |

\*Includes chronic lymphocytic leukemia, Waldenström's macroglobulinemia, mantle cell lymphoma, follicular lymphoma, marginal zone lymphoma, hairy cell leukemia, diffuse large B-cell lymphoma, and Richter's transformation.<sup>1</sup>

### IMPORTANT SAFETY INFORMATION (continued)

#### WARNINGS AND PRECAUTIONS (continued)

##### Cytopenias

Grade 3 or 4 cytopenias, including neutropenia (21%), thrombocytopenia (8%) and anemia (8%) based on laboratory measurements, developed in patients treated with BRUKINSA. Grade 4 neutropenia occurred in 10% of patients, and Grade 4 thrombocytopenia occurred in 2.5% of patients.

Monitor complete blood counts regularly during treatment and interrupt treatment, reduce the dose, or discontinue treatment as warranted. Treat using growth factor or transfusions, as needed.

##### Second Primary Malignancies

Second primary malignancies, including non-skin carcinoma, have occurred in 14% of patients treated with BRUKINSA. The most frequent second primary malignancy was non-melanoma skin cancers (8%), followed by other solid tumors in 7% of the patients (including melanoma in 1% of patients) and hematologic malignancies (0.7%). Advise patients to use sun protection and monitor patients for the development of second primary malignancies.

##### Cardiac Arrhythmias

Serious cardiac arrhythmias have occurred in patients treated with BRUKINSA. Atrial fibrillation and atrial flutter were reported in 4.4% of patients treated with BRUKINSA, including Grade 3 or higher cases in 1.9% of patients. Patients with cardiac risk factors, hypertension, and acute infections may be at increased risk. Grade 3 or higher ventricular arrhythmias were reported in 0.3% of patients.

Monitor for signs and symptoms of cardiac arrhythmias (e.g., palpitations, dizziness, syncope, dyspnea, chest discomfort), manage appropriately, and consider the risks and benefits of continued BRUKINSA treatment.

## MANAGEMENT OF AEs OF SPECIAL INTEREST

| RECOMMENDATIONS FOR AEs OF SPECIAL INTEREST <sup>5,6</sup> |  |
|--|--|
| Rash   | Recommendations include moisturizing skin creams, antihistamine medications, and/or steroids.  |
| Diarrhea   | Recommendations include medications that may prevent and treat diarrhea, such as loperamide or a combination of diphenoxylate and atropine. Avoiding the following may help manage mild diarrhea: caffeine, alcohol, dairy, fat, fiber, orange juice, prune juice, and spicy foods.                                  |
| Fatigue  | Recommendations include lifestyle changes, dietary changes, working with a physical therapist or personal trainer, and medications or supplements that could help relieve fatigue. The following mind-body strategies may also help to reduce fatigue: yoga, acupuncture, massage, music therapy, and touch therapy. |
| Headache   | Recommendations include pain relievers, tricyclic antidepressants, triptans, steroids, and antibiotics. The following may help reduce the number and severity of headaches: more sleep, changing diet, and reducing stress.  |

| RECOMMENDATIONS FOR AFIB/FLUTTER <sup>7</sup> |  |
|---|--|
| Afib/flutter                                  | Recommendations include anticoagulation therapy after estimating the patient's risk of a thromboembolic event or major bleed. There is an increased risk of bleeding when combining BTKis with antiplatelet or anticoagulation therapy. Advise patients on antiplatelet or anticoagulation therapy to avoid taking medications such as NSAIDs, aspirin, vitamin E, fish oils, or flaxseed. |

AEs=adverse events; afib=atrial fibrillation; BTKi=Bruton's tyrosine kinase inhibitor; NSAIDs=non-steroidal anti-inflammatory drugs.

Please also see dose modifications specific to BRUKINSA on the next page.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information.



# FLEXIBILITY TO MODIFY DOSE IN SMALL INCREMENTS

## ARs That Require Dose Modifications<sup>2</sup>

- Grade 3 or Grade 4 febrile neutropenia
- Platelet count decreased to 25,000-50,000/mm<sup>3</sup> with significant bleeding
- Neutrophil count decreased to <500/mm<sup>3</sup>\*
- Platelet count decreased to <25,000/mm<sup>3</sup>\*
- Severe or life-threatening nonhematological toxicities<sup>†</sup>

Asymptomatic lymphocytosis in CLL and MCL should not be regarded as an adverse reaction, and these patients should continue taking BRUKINSA.<sup>2</sup>

## Recommended Dose Modifications by Occurrence for Grade ≥3 ARs<sup>2</sup>

| Recommended Dose  | 1st Occurrence        | 2nd Occurrence  | 3rd Occurrence                          | 4th Occurrence     |
|---|-----------------------|---|---|--------------------|
| <b>320 mg total dose</b><br>(160 mg twice daily or 320 mg once daily) | <b>No dose change</b> | <b>Reduce to ½ tablet twice daily or 1 tablet daily (160 mg total dose)</b> | <b>Reduce to ½ tablet daily (80 mg)</b> | <b>Discontinue</b> |
|   |                       |   |   |                    |

\*Lasting more than 10 consecutive days.<sup>2</sup>

<sup>†</sup>Evaluate the benefit-risk before resuming treatment at the same dosage for Grade 4 nonhematological toxicity.<sup>2</sup>

- BRUKINSA 160 mg tablets are scored, making them easy for patients to split

**No dose exchange required for dose modification; simply reduce the number of tablets<sup>2</sup>**

Refer to the obinutuzumab Prescribing Information for management of obinutuzumab toxicities.<sup>2</sup>

## IMPORTANT SAFETY INFORMATION (continued)

### WARNINGS AND PRECAUTIONS (continued)

#### Hepatotoxicity, Including Drug-Induced Liver Injury

Hepatotoxicity, including severe, life-threatening, and potentially fatal cases of drug-induced liver injury (DILI), has occurred in patients treated with Bruton tyrosine kinase inhibitors, including BRUKINSA.

Evaluate bilirubin and transaminases at baseline and throughout treatment with BRUKINSA. For patients who develop abnormal liver tests after BRUKINSA, monitor more frequently for liver test abnormalities and clinical signs and symptoms of hepatic toxicity. If DILI is suspected, withhold BRUKINSA. Upon confirmation of DILI, discontinue BRUKINSA.

# LOW RATES OF DOSE REDUCTIONS AND TREATMENT DISCONTINUATIONS

## Rates Across BRUKINSA Studies<sup>2</sup>

| Dose Reductions Due to ARs Ranged From |
|--|
| <b>0.8% - 11%</b>                      |

| Discontinuations Due to ARs Ranged From |
|---|
| <b>2% - 17%</b>                         |

|   | Dose Reduction Rates Due to ARs | Discontinuation Rates Due to ARs | Median Duration of Treatment |
|---|---------------------------------|----------------------------------|------------------------------|
| CLL (TN) <sup>12,8</sup>                                  | 8%                              | 8%                               | 26 months                    |
| CLL (R/R) <sup>2,9</sup>                                  | 11%                             | 13%                              | 28 months                    |
| WM (TN, R/R) <sup>11,2</sup>                              | 11%                             | 2%                               | 25 months                    |
| MCL (R/R) <sup>1,2</sup>                                  | 0.8%                            | 7%                               | 17.5 months                  |
| MZL (R/R) <sup>1,2</sup>                                  | 2.3%                            | 6%                               | 14.5 months                  |
| FL (R/R) in combination with obinutuzumab <sup>2,10</sup> | 9%                              | 17%                              | 12.2 months                  |

<sup>1</sup>Cohort 1.<sup>2</sup>

## Neutropenia-Related Discontinuations<sup>1,2</sup>

No patients discontinued due to neutropenia in the TN CLL and R/R MCL and MZL studies. One patient in both the WM and FL studies and 2 patients in the R/R CLL study discontinued due to neutropenia. Patients in studies received growth factor support as needed.

CLL=chronic lymphocytic leukemia; FL=follicular lymphoma; MCL=mantle cell lymphoma; MZL=marginal zone lymphoma; R/R=relapsed/refractory; TN=treatment naive; WM=Waldenström's macroglobulinemia.

**Please see additional Important Safety Information throughout and accompanying full Prescribing Information.**



# myBeOneSupport™ Patient Assistance Program

Assisting you in providing support for eligible patients  
after BRUKINSA has been prescribed

For patient enrollment and other program services,  
visit **myBeOneSupport.com** or call **1-833-234-4363**,  
M-F 8 AM - 8 PM ET, and speak with a dedicated Oncology Nurse Advocate.

## IMPORTANT SAFETY INFORMATION (continued)

### WARNINGS AND PRECAUTIONS (continued)

#### Embryo-Fetal Toxicity

Based on findings in animals, BRUKINSA can cause fetal harm when administered to a pregnant woman. Administration of zanubrutinib to pregnant rats during the period of organogenesis caused embryo-fetal toxicity, including malformations at exposures that were 5 times higher than those reported in patients at the recommended dose of 160 mg twice daily. Advise women to avoid becoming pregnant while taking BRUKINSA and for 1 week after the last dose. Advise men to avoid fathering a child during treatment and for 1 week after the last dose. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

#### ADVERSE REACTIONS

The most common adverse reactions ( $\geq 30\%$ ), including laboratory abnormalities, in patients who received BRUKINSA (N=1729) are decreased neutrophil count (51%), decreased platelet count (41%), upper respiratory tract infection (38%), hemorrhage (32%), and musculoskeletal pain (31%).

#### DRUG INTERACTIONS

**CYP3A Inhibitors:** When BRUKINSA is coadministered with a strong CYP3A inhibitor, reduce BRUKINSA dose to 80 mg once daily. For coadministration with a moderate CYP3A inhibitor, reduce BRUKINSA dose to 80 mg twice daily.

**CYP3A Inducers:** Avoid coadministration with strong or moderate CYP3A inducers. Dose adjustment may be recommended with moderate CYP3A inducers.

#### SPECIFIC POPULATIONS

**Hepatic Impairment:** The recommended dose of BRUKINSA for patients with severe hepatic impairment is 80 mg orally twice daily.

**Please see additional Important Safety Information throughout and accompanying full Prescribing Information.**

**References:** **1.** Data on file. BeiGene USA, Inc. **2.** BRUKINSA. Package insert. BeOne Medicines USA, Inc.; 2025. **3.** IMBRUVICA. Package insert. Pharmacyclics LLC, Janssen Biotech, Inc; 2024. **4.** CALQUENEC. Package insert. AstraZeneca Pharmaceuticals LP; 2025. **5.** American Cancer Society. Managing cancer-related side effects. Cancer.org website. Accessed May 20, 2025. <https://www.cancer.org/cancer/managing-cancer/side-effects.html> **6.** Bernstein CA. Evaluation of headache in patients with cancer. *Cancer*. 2021;127(23):4368-4375. **7.** American College of Cardiology. Anticoagulation for atrial fibrillation (AFib) in patients receiving Bruton tyrosine kinase (BTK) inhibitors. Created May 20, 2021. Accessed December 17, 2024. Reprinted with permission. © 2022 American Society of Clinical Oncology. All rights reserved. <https://acc.bravais.com/s/CNJBxHNRDl2G7lxbkcSy> **8.** Tam CS, Brown JR, Kahl BS, et al. Zanubrutinib versus bendamustine and rituximab in untreated chronic lymphocytic leukaemia and small lymphocytic lymphoma (SEQUOIA): a randomised, controlled, phase 3 trial. *Lancet Oncol*. 2022;23(8):1031-1043. **9.** Brown JR, Eichhorst B, Hillmen P, et al. Zanubrutinib or ibrutinib in relapsed or refractory chronic lymphocytic leukemia. *N Engl J Med*. 2023;388(4):319-332. **10.** Zinzani PL, Mayer J, Flowers CR, et al. ROSEWOOD: a phase II randomized study of zanubrutinib plus obinutuzumab versus obinutuzumab monotherapy in patients with relapsed or refractory follicular lymphoma. *J Clin Oncol*. 2023;41(33):5107-5117.

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