FOR ADULT PATIENTS WITH **R/R MARGINAL ZONE LYMPHOMA (MZL)***[1]

THE BTK INHIBITOR THAT DELIVERS DEEP AND SUSTAINED RESPONSES[1,2]

BRUKINSA® (zanubrutinib) is a kinase inhibitor indicated for the treatment of adult patients with:

- 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.

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

24-hour inhibition of BTK was maintained at 100% in PBMCs and 94% to 100% in lymph nodes when taken at the recommended total daily dose of 320 mg. The clinical significance of 100% inhibition has not been established.[1,2]

Powerful Responses Regardless of Risk Factor or MZL Subtype

Response rates

MAGNOLIA (STUDY **214**; N=66)—CT-based*†[1,3]

56% ORR (95% CI: 43, 68) **20%** CR **36%** PR

MAGNOLIA (STUDY **214**; N=66)—PET-based*†‡[1,3]

67% ORR (95% CI: 54, 78) **26%** CR **41%** PR

Median time to response in **MAGNOLIA** (Study **214**) was 2.9 months (range: 1.8-11.1).[1]

STUDY **003** (MZL; N=20)—CT-based*[1,4]

80% ORR (95% CI: 56, 94) **20%** CR **60%** PR

Median time to response in Study **003** was 2.9 months (range: 2.6-23.1).[1]

Safety in MZL Consistent With Established Profile

Dose reductions due to adverse reactions[1]

2.3% of patients

Discontinuation rate due to adverse reactions[1]

6% of patients

Serious adverse reactions, including fatal events, have occurred with BRUKINSA, including hemorrhage, infections, cytopenias, second primary malignancies, and cardiac arrhythmias. The most common adverse reactions, including laboratory abnormalities, in ≥30% of patients included neutrophil count decreased, upper respiratory tract infection, platelet count decreased, hemorrhage, lymphocyte count decreased, rash, and musculoskeletal pain.

Flexible Dosing to Meet Patient Needs

2 flexible dosing options[1]

BRUKINSA can be taken as 160 mg twice daily or 320 mg once daily

No dose adjustments needed with several common medications[1]

- Proton pump inhibitors
- H2-receptor antagonists

No dose exchange required for dose modification[1]

Dose modification for ≥Grade 3 adverse reactions only requires reduction in number of capsules taken daily

Please see additional Important Safety Information on the next page, and accompanying full Prescribing Information.

*The efficacy of BRUKINSA was assessed by IRC in 2 clinical trials that included a total of 88 adult patients with MZL who received at least 1 prior therapy. Tumor response was according to the 2014 Lugano classification for both studies, and the primary efficacy endpoint was ORR as assessed by IRC. Study BGB-3111-214 **MAGNOLIA** (Study **214**): N=66, Phase 2, open-label, multicenter, single-arm trial; PET scans were required for response assessment. Study BGB-3111-AU-003 (Study **003**): N=20, Phase 1/2, open-label, global, multicenter, single-arm trial; PET scans were not required for response assessment and the majority of patients were assessed mostly using CT scans.

†Two patients in **MAGNOLIA** (Study **214**) were not evaluable for efficacy due to central confirmation of MZL transformation to diffuse large B-cell lymphoma.

‡55 patients were assessed by PET scan, with the remainder assessed by CT scan.

BTK=Bruton's tyrosine kinase; CI=confidence interval; CR=complete response; CT=computed tomography; IRC=independent review committee; ORR=overall response rate; PBMCs=peripheral blood mononuclear cells; PET=positron emission tomography; PR=partial response; R/R=relapsed/refractory.

Brukinsa® zanubrutinib 80 mg capsules

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IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hemorrhage
Fatal and serious hemorrhagic events have occurred in patients with hematological malignancies treated with BRUKINSA monotherapy. Grade 3 or higher hemorrhage events including intracranial and gastrointestinal hemorrhage, hematuria and hemothorax have been reported in 3.4% of patients treated with BRUKINSA monotherapy. Hemorrhage events of any grade occurred in 35% of patients treated with BRUKINSA monotherapy.

Bleeding events have occurred in patients with and without concomitant antiplatelet or anticoagulation therapy. Co-administration 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 pre- and post-surgery depending upon the type of surgery and the risk of bleeding.

Infections
Fatal and serious infections (including bacterial, viral, or fungal) and opportunistic infections have occurred in patients with hematological malignancies treated with BRUKINSA monotherapy. Grade 3 or higher infections occurred in 27% of patients, most commonly pneumonia. Infections due to hepatitis B virus (HBV) reactivation have occurred.

Consider prophylaxis for herpes simplex virus, pneumocystis jiroveci 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.

Cytopenias
Grade 3 or 4 cytopenias, including neutropenia (26%), thrombocytopenia (11%) and anemia (8%) based on laboratory measurements, were reported in patients treated with BRUKINSA monotherapy. Grade 4 neutropenia occurred in 13% of patients, and Grade 4 thrombocytopenia occurred in 3.6% 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 monotherapy. The most frequent second primary malignancy was non-melanoma skin cancer reported in 8% of patients. Other second primary malignancies included malignant solid tumors (4.0%), melanoma (1.7%) and hematologic malignancies (1.2%). Advise patients to use sun protection, and monitor patients for the development of second primary malignancies.

Cardiac Arrhythmias
Atrial fibrillation and atrial flutter were reported in 3.2% of patients treated with BRUKINSA monotherapy. Patients with cardiac risk factors, hypertension and acute infections may be at increased risk. Grade 3 or higher events were reported in 1.1% of patients treated with BRUKINSA monotherapy. Monitor signs and symptoms for atrial fibrillation and atrial flutter and manage as appropriate.

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, including laboratory abnormalities, in ≥ 30% of patients who received BRUKINSA (N=847) included decreased neutrophil count (54%), upper respiratory tract infection (47%), decreased platelet count (41%), hemorrhage (35%), decreased lymphocyte count (31%), rash (31%) and musculoskeletal pain (30%).

DRUG INTERACTIONS

CYP3A Inhibitors: When BRUKINSA is co-administered with a strong CYP3A inhibitor, reduce BRUKINSA dose to 80 mg once daily. For co-administration with a moderate CYP3A inhibitor, reduce BRUKINSA dose to 80 mg twice daily.

CYP3A Inducers: Avoid co-administration with moderate or strong CYP3A inducers.

SPECIFIC POPULATIONS

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

INDICATIONS

- BRUKINSA is a kinase inhibitor indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.
- BRUKINSA is indicated for the treatment of adult patients with relapsed or refractory marginal zone lymphoma (MZL) who have received at least one anti-CD20-based regimen.

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

- BRUKINSA is indicated for the treatment of adult patients with Waldenström's macroglobulinemia (WM).

Please see full Prescribing Information including Patient Information.

References: 1. BRUKINSA. Package insert. BeiGene, Ltd; 2021. **2.** Tam C, Trotman J, Opat S, et al. Phase 1 study of the selective BTK inhibitor zanubrutinib in B-cell malignancies and safety and efficacy evaluation in CLL. *Blood*. 2019;134(11):851-859. **3.** BeiGene. Study of zanubrutinib (BGB-3111) in participants with marginal zone lymphoma (MAGNOLIA). ClinicalTrials.gov website. NCT03846427. Last updated May 19, 2021. Accessed June 15, 2021. https://clinicaltrials.gov/ct2/show/NCT03846427 **4.** BeiGene. Study of the safety and pharmacokinetics of BGB-3111 in subjects with B-cell lymphoid malignancies. ClinicalTrials.gov website. NCT02343120. Last updated May 19, 2021. Accessed May 24, 2021. https://clinicaltrials.gov/ct2/show/NCT02343120

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