In Previously Treated Mantle Cell Lymphoma (MCL)*

THE BTK INHIBITOR DEMONSTRATED TO PROVIDE COMPLETE AND SUSTAINED INHIBITION[1,2]

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]

*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 a confirmatory trial.

Powerful Responses With Consistent Results†

STUDY **206** | PET-BASED[1]

84% ORR (95% CI: 74, 91)

59% CR

19.5 mo MEDIAN DOR (95% CI: 16.6, NE)

STUDY **003** | CT-BASED[1]

84% ORR (95% CI: 67, 95)

22% CR

18.5 mo MEDIAN DOR (95% CI: 12.6, NE)

Median follow-up time was 18.4 months for Study 206 and 18.8 months for Study 003[3]

Demonstrated Safety Profile

Dose reductions due to adverse reactions[1]

0.8% (1/118) of patients

Discontinuation rate due to adverse reactions[1]

7% (8/118) of patients

Median duration of treatment: 17.5 months (range: 0.2-33.9 months)[3]

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 (≥20%) included neutrophil count decreased, platelet count decreased, upper respiratory tract infection, white blood cell count decreased, hemoglobin decreased, rash, bruising, diarrhea, and cough.

Flexible Dosing to Meet Patient Needs

2 flexible dosing options[1]

BRUKINSA® (zanubrutinib) can be taken as 160 mg twice daily or 320 mg once daily

No dose adjustments needed with several common medications[1,3,4]

- Gastric acid reducing agents
- Anticlotting medications‡

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 IRC-assessed in 2 clinical trials that included a total of 118 adult patients with MCL who received at least 1 prior therapy. Study **206**: N=86, Phase 2, open-label, multicenter, single-arm trial; PET scans were required for response assessment. Study **003**: N=32, 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 by CT scan.

‡BRUKINSA was allowed to be coadministered in clinical trials with antiplatelets and anticoagulants (as long as INR was ≤1.5 and aPTT ≤1.5 x ULN).

aPTT=activated partial thromboplastin time; BTK=Bruton's tyrosine kinase; CI=confidence interval; CR=complete response; CT=computed tomography; DOR=duration of response; INR=International Normalized Ratio; IRC=independent review committee; NE=not estimable; ORR=overall response rate; PBMCs=peripheral blood mononuclear cells; PET=positron emission tomography; ULN=upper limit of normal.

Brukinsa® zanubrutinib 80mg 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 bleeding events including intracranial and gastrointestinal hemorrhage, hematuria and hemothorax have been reported in 2% of patients treated with BRUKINSA monotherapy. Bleeding events of any grade, including purpura and petechiae, occurred in 50% 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 23% of patients treated with BRUKINSA monotherapy. The most common Grade 3 or higher infection was 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 (27%), thrombocytopenia (10%) and anemia (8%) based on laboratory measurements, were reported in patients treated with BRUKINSA monotherapy.

Monitor complete blood counts during treatment and treat using growth factor or transfusions, as needed.

Second Primary Malignancies
Second primary malignancies, including non-skin carcinoma, have occurred in 9% of patients treated with BRUKINSA monotherapy. The most frequent second primary malignancy was skin cancer (basal cell carcinoma and squamous cell carcinoma of skin), reported in 6% of patients. Advise patients to use sun protection.

Cardiac Arrhythmias
Atrial fibrillation and atrial flutter have occurred in 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 0.6% 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 at least 1 week after the last dose. Advise men to avoid fathering a child during treatment and for at least 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 in > 10% of patients who received BRUKINSA were decreased neutrophil count (53%), decreased platelet count (39%), upper respiratory tract infection (38%), decreased white blood cell count (30%), decreased hemoglobin (29%), rash (25%), bruising (23%), diarrhea (20%), cough (20%), musculoskeletal pain (19%), pneumonia (18%), urinary tract infection (13%), hematuria (12%), fatigue (11%), constipation (11%), and hemorrhage (10%).

Of the 118 patients with MCL treated with BRUKINSA, 8 (7%) patients discontinued treatment due to adverse reactions in the trials. The most frequent adverse reaction leading to treatment discontinuation was pneumonia (3.4%). One (0.8%) patient experienced an adverse reaction leading to dose reduction (hepatitis B).

DRUG INTERACTIONS

CYP3A Inhibitors: When BRUKINSA is co-administered 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 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.

INDICATION

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.

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 a confirmatory trial.

Please see full Prescribing Information including Patient Information.

References: 1. BRUKINSA [package insert]. BeiGene, Ltd; 2019. **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.** Data on file. BeiGene, Ltd. 2019. **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 31, 2019. Accessed September 12, 2019. https://clinicaltrials.gov/ct2/show/NCT02343120

Brukinsa® zanubrutinib 80 mg capsules

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