BRUKINSA™ & BTK Inhibition

I. What is BRUKINSA?

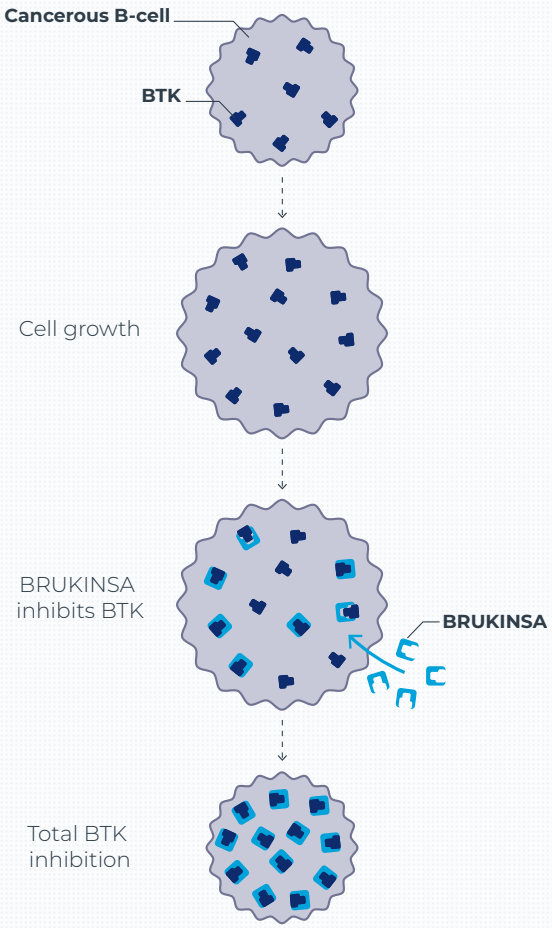
BRUKINSA (zanubrutinib) is an inhibitor of Bruton's tyrosine kinase (BTK) indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy. This indication is approved by the U.S. FDA under accelerated approval based on overall response rate.*

BRUKINSA was discovered and developed by BeiGene, a global commercial-stage biopharmaceutical company focused on developing and commercializing innovative molecularly-targeted and immuno-oncology drugs for the treatment of cancer.

*Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

II. How does BRUKINSA work?

When cancer forms in B-cells, they often have too much BTK, which causes the cancerous cells to grow. BRUKINSA is a BTK inhibitor that blocks unusual BTK activity associated with malignant B-cell growth and survival.



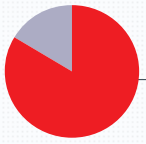
III. Efficacy in MCL

The efficacy of BRUKINSA was evaluated globally in two clinical trials, which included a total of 118 adult patients with MCL who had received at least one prior therapy. BRUKINSA was given orally at a dose of 320 mg daily until disease progression or unacceptable toxicity.

BRUKINSA achieved an overall response rate (ORR) of more than 80% in both studies.[i]

Phase 2[i]:
NCT03206970

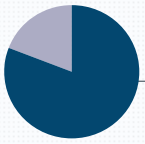
- **83.7%** of patients achieved an overall response. Of these:
  - **59.3%** achieved complete response
  - **24.4%** achieved partial response
- On average, patients responded to treatment with BRUKINSA for **19.5** months



83.7%
patients achieved an overall response

Phase 1/2[i]:
NCT02343120

- **84.4%** of patients achieved an overall response. Of these:
  - **21.9%** achieved complete response
  - **62.5%** achieved partial response
- On average, patients responded to treatment with BRUKINSA for **18.5** months



84.4%
patients achieved an overall response

Overall response rate was assessed by an independent review committee. ORR measures the proportion of patients whose tumors became smaller after exposure to treatment.

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Brukinsa™ 80mg zanubrutinib

IV. Dosing and Administration

The recommended dose of BRUKINSA is 160 mg taken orally twice daily or 320 mg taken orally once daily until disease progression or unacceptable toxicity.

BRUKINSA can be taken with or without food. Advise patients to swallow capsules whole with water. Advise patients not to open, break or chew the capsules. If a dose of BRUKINSA is missed, it should be taken as soon as possible on the same day with a return to the normal schedule the following day.[i]

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.

[i]BRUKINSA (zanubrutinib) Prescribing Information. beigene.com/PDF/BRUKINSAUSPI.pdf. BeiGene, Ltd; 2019.
[ii]Pazdur R. Endpoints for Assessing Drug Activity in Clinical Trials. The Oncologist April 2008 vol. 13 Supplement 2 19-21.

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Brukinsa™ 80mg zanubrutinib capsules

IMPORTANT SAFETY INFORMATION (CONTINUED)

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 neutrophil count decreased (53%), platelet count decreased (39%), upper respiratory tract infection (38%), white blood cell count decreased (30%), hemoglobin decreased (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%).

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.

[i]BRUKINSA (zanubrutinib) Prescribing Information. beigene.com/PDF/BRUKINSAUSPI.pdf. BeiGene, Ltd; 2019.
[ii]Pazdur R. Endpoints for Assessing Drug Activity in Clinical Trials. The Oncologist April 2008 vol. 13 Supplement 2 19-21.

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