PRESCRIBING INFORMATION

BRUKINSA®▼(zanubrutinib) 80 mg hard capsules for oral use
This medicinal product is subject to additional monitoring. This will facilitate identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. Refer to Section 4.8 of the SmPC for how to report adverse reactions.
Presentation: Each hard capsule contains 80 mg of zanubrutinib.
Indication: BRUKINSA as monotherapy is indicated for the treatment of adult patients with Waldenström's macroglobulinaemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy.
BRUKINSA as monotherapy is indicated for the treatment of adult patients with marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based therapy.
BRUKINSA as monotherapy is indicated for the treatment of adult patients with chronic lymphocytic leukemia (CLL).
BRUKINSA as monotherapy is indicated for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.
Dosage and method of administration: *Recommended dosage:* The recommended total daily dose of BRUKINSA is 320 mg. The daily dose may be taken either once daily (four 80 mg capsules) or divided into two doses of 160 mg twice daily (two 80 mg capsules). The capsules can be taken with or without food. Patients should be instructed to swallow the capsules whole with water, and not to open, break or chew the capsules. Treatment with BRUKINSA should be continued until disease progression or unacceptable toxicity. *Recommended dosage modification for adverse reactions*: For ≥Grade 3 non-haematological toxicities, Grade 3 febrile neutropenia, Grade 3 thrombocytopenia with significant bleeding, Grade 4 neutropenia (lasting >10 consecutive days), or Grade 4 thrombocytopenia (lasting >10 consecutive days), at first occurrence, interrupt BRUKINSA. Once toxicity has resolved to ≤Grade 1 or baseline, resume at 320 mg once daily or 160 mg twice daily. At second occurrence, interrupt BRUKINSA. Once toxicity has resolved to ≤Grade 1 or baseline, resume at 160 mg once daily or 80 mg twice daily. At third occurrence, interrupt BRUKINSA. Once toxicity has resolved to ≤Grade 1 or baseline, resume at 80 mg once daily. At fourth occurrence, discontinue BRUKINSA. Asymptomatic lymphocytosis should not be regarded as an adverse reaction, and these patients should continue taking BRUKINSA. *Recommended dosage modification when co-administered with other medicinal products*: With strong CYP3A inhibitors (e.g., posaconazole, voriconazole, ketoconazole, itraconazole, clarithromycin, indinavir, lopinavir, ritonavir, telaprevir), the recommended dose of BRUKINSA is 80 mg once daily. With moderate CYP3A inhibitors (e.g., erythromycin, ciprofloxacin, diltiazem, dronedarone, fluconazole, verapamil, aprepitant, imatinib, grapefruit juice, Seville oranges), the recommended dose of BRUKINSA is 160 mg for the duration of inhibitor use. Avoid use of strong (e.g., carbamazepine, phenytoin, rifampin, St. John's wort) and moderate (e.g., bosentan, efavirenz, etravirine, modafinil, nafcillin) CYP3A inducers. *Paediatric population (<18 years of age)*: The safety and efficacy of BRUKINSA in children and adolescents have not been established. No data are available. *Elderly population (≥65 years of age)*: No dose adjustment is required. *Renal impairment:* No dose adjustment is recommended in patients with mild to moderate renal impairment. There are limited data in patients with severe renal impairment. *Hepatic impairment*: No dose adjustment is recommended in patients with mild or moderate hepatic impairment. The recommended dose of BRUKINSA for patients with severe hepatic impairment is 80 mg twice daily.
Contraindications: Hypersensitivity to the active substance or to any of the excipients. **Warnings and precautions**: *Haemorrhage*: Serious and fatal haemorrhagic events have occurred in patients treated with BRUKINSA. BRUKINSA may increase the risk of haemorrhage in patients receiving antiplatelet or anticoagulant therapies and patients should be monitored for signs of bleeding. Dose modification may be necessary for Grade 3 or greater adverse reactions as recommended in Section 4.2 of the SmPC. Warfarin or other vitamin K antagonists should not be administered concomitantly with BRUKINSA. Patients should be monitored for signs and symptoms of bleeding and monitor complete blood counts. Consider the benefit-risk of withholding BRUKINSA for 3 to 7 days pre- and post-surgery depending upon the type of surgery and the risk of bleeding. *Infections*: Fatal and non-fatal infections (including bacterial, viral, fungal infections, or sepsis) and opportunistic infections (e.g., herpes viral, cryptococcal, aspergillus and pneumocystis jiroveci infections have occurred in patients treated with BRUKINSA. The most common Grade 3 or higher infection was pneumonia. Infections due to hepatitis B virus (HBV) reactivation have also occurred. Before initiating treatment with BRUKINSA, patients' HBV status should be established. Consultation with a liver disease expert physician is recommended for patients who test positive for HBV or have positive hepatitis B serology, before initiating treatment. Patients should be monitored and managed according to the medical standards to prevent hepatitis B reactivation. Consider prophylaxis according to standard of care in patients who are at increased risk for infections. Patients should be monitored for signs and symptoms of infection and treat appropriately. *Cytopenia*: Grade 3 or 4 cytopenias including neutropenia, thrombocytopenia, and anaemia based on laboratory measurements were reported in patients treated with BRUKINSA. Monitor complete blood counts monthly during treatment. *Second primary malignancies*: Second primary malignancies, including non-skin carcinoma have occurred in patients treated with BRUKINSA. The most frequent second primary malignancy was skin cancer (basal cell carcinoma and squamous cell carcinoma of skin). Advise patients to use sun protection. *Atrial fibrillation and flutter:* Atrial fibrillation and atrial flutter have occurred in patients treated with BRUKINSA, particularly patients with cardiac risk factors, hypertension, acute infections and elderly (≥ 65 years). Monitor signs and symptoms for atrial fibrillation and atrial flutter and manage as appropriate. *Tumour lysis syndrome:* Tumour lysis syndrome has been infrequently reported with BRUKINSA therapy, particularly in patients who were treated for CLL. Assess relevant risks (e.g., high tumour burden or blood uric acid level) and take appropriate precautions. Monitor patients closely and treat as appropriate. *Driving and operating machinery*: BRUKINSA has no or negligible influence in the ability to drive and use machines. Fatigue, dizziness, and asthenia have been reported in some patients taking BRUKINSA and should be considered when assessing a patient's ability to drive or operate machines. *Women of childbearing potential and pregnancy*: Women should avoid becoming pregnant while taking BRUKINSA and for up to 1 month after ending treatment. Women of childbearing potential must use highly effective contraceptive measures while taking BRUKINSA and for up to 1 month after stopping treatment. Pregnancy testing is recommended for women of reproductive potential prior to initiating therapy. BRUKINSA should not be used during pregnancy. Breast-feeding should be discontinued during treatment with BRUKINSA. **Interaction with other medicinal products and other forms of interaction:** See recommended dose modification in **Dosage and method of administration** section of the SmPC. The coadministration of oral P-gp substrates with a narrow therapeutic index (e.g., digoxin) should be done with caution as BRUKINSA may increase their concentrations.
Adverse reactions: The most commonly occurring adverse reactions were upper respiratory tract infection, bruising, haemorrhage/haematoma, neutropenia, musculoskeletal pain, rash, pneumonia, diarrhoea and cough. The most common Grade 3 or higher adverse reactions were neutropenia, pneumonia, hypertension, thrombocytopenia, anaemia and haemorrhage/haematoma. **Refer to the full SmPC for additional information and other adverse reactions**.
Legal category: POM. **Package quantities**: 1 bottle containing 120 caps x 80 mg. **Costs**: United Kingdom: £4,928.65. **Marketing Authorisation Holder**: United Kingdom: BeiGene UK Ltd, c/o REGUS, 2 Kingdom Street, London W2 6BD, United Kingdom. **Marketing Authorisation Number**: United Kingdom: PLGB 53789/0002. **Further information available from**: medicalinformationEU@beigene.com. **Date of First Authorisation**: 06 December 2021. **Doc Ref** 0824-BRU-PRC-006. **Date of preparation**: December 2024

Adverse events should be reported.
United Kingdom: **Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme found at www.mhra.gov.uk/yellowcard.**
Adverse events should also be reported to BeiGene at adverse_events@beigene.com

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