

Zanubrutinib (Brukinsa®) treatment for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma

Description:

- The purpose of this PQI is to discuss clinical considerations around the use of zanubrutinib to optimize outcomes for patients with chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

Background:

- Zanubrutinib is a highly selective, covalent, and irreversible inhibitor of Bruton's tyrosine kinase (BTK)
- FDA approved indications include (but are not limited to):
 - Treatment of adults with CLL or SLL
- Most common adverse reactions ($\geq 30\%$; including laboratory abnormalities): neutrophil count decreased, platelet count decreased, upper respiratory tract infection, hemorrhage, and musculoskeletal pain

PQI Process:

Upon receipt of an order for Zanubrutinib for CLL/SLL:

- Verify patient dose to be 160 mg by mouth every 12 hours or 320 mg by mouth once daily with or without food
 - Selection of dosing strategy should take into account pill burden and patient's ability to adhere to therapy
 - Patient comorbidities may make zanubrutinib a safer option vs a different BTK inhibitor (ex. history of atrial fibrillation [Afib], recent hemorrhage, hypertension, concomitant PPI or H2 receptor antagonists)²
- Dosage forms and strengths:
 - Capsules: 80 mg – should not be broken or opened
 - Tablets: 160 mg with functional scoring
- Modify zanubrutinib dose accordingly if co-administered with:
 - Strong CYP3A inhibitor – 80 mg once daily
 - Moderate CYP3A inhibitor – 80 mg twice daily
 - Moderate or Strong CYP3A inducer – avoid concomitant use
 - If a moderate CYP3A inducer cannot be avoided, the dose may be increased to 320 mg twice daily.
 - Reduce dose to 80 mg twice daily in patients with severe hepatic impairment (Child-Pugh Class C)
- Consider prophylaxis for herpes simplex virus, *Pneumocystis jirovecii* pneumonia, and other infections according to standard of care in patients at increased risk for infections
- If a dose is missed, it should be taken as soon as possible on the same day then return to the normal schedule the following day.

- Verify monitoring parameters:
 - CBC with differential, hepatic function
 - Signs/symptoms of Afib/flutter, bleeding, or infections including opportunistic infections
- Asymptomatic lymphocytosis should not be regarded as an adverse reaction, and these patients should continue taking zanubrutinib
- Consider the benefit-risk of withholding zanubrutinib for 3-7 days before and after surgery depending upon the type of surgery and the risk of bleeding
- See full prescribing information for dose modifications with Grade 3 or worse adverse effects

Patient-Centered Activities:

- Provide [Patient Education Sheet](#) and review with patient
- Counsel to administer orally, review once a day vs twice a day dosing
- Proper sign/symptom monitoring
- Evaluate if patients have missed any doses between cycles; consider reminders, calendars, pill box, etc.
- Patient Assistance:
 - [NCODA Financial Assistance Tool](#)
 - [myBeOne Patient Support Program](#)

References:

1. BRUKINSA® (zanubrutinib) [package insert]. Pennington, NJ: BeOne Medicines USA, Inc.;2025.
2. Shadman M, et al. P633: UPDATED SAFETY AND EFFICACY RESULTS OF ZANUBRUTINIB IN PATIENTS WITH B-CELL MALIGNANCIES WHO ARE INTOLERANT OF IBRUTINIB AND/OR ACALABRUTINIB. Hemasphere. 2023 Aug 8;7(Suppl):e70152b3. doi: 10.1097/01.HS9.