PRACTICE AID

Dosing, Drug–Drug Interactions, and Safety Monitoring With BTK Inhibitors in CLL/SLL

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Covalent BTK Inhibitors

	Standard Dose	Dosage Forms	Strong CYP3A Inhibitors	Moderate CYP3A Inhibitors	Moderate or Strong CYP3A Inducers	Gastric Acid–Reducing Agents	Safety Monitoring
Ibrutinib[1]	420 mg once daily	Capsules	Reduce ibrutinib dose to 140 mg once daily; for short-term use, consider interrupting ibrutinib	Reduce ibrutinib dose to 280 mg once daily	Avoid use	No dosage adjustment recommended	Monitor for atrial fibrillation, infections, bleeding, cytopenias, and TLS
Acalabrutinib Maleate Salt[2]	100 mg every 12 hours	Tablets (IR film-coated tablet; capsule formulation has been discontinued)[3]	Avoid use	Reduce acalabrutinib dose to 100 mg once daily	Avoid use; if necessary, increase acalabrutinib dose to 200 mg twice daily	Tablets can be used regardless of use of PPIs and ingestion of food	Monitor for atrial fibrillation, infections, bleeding, and cytopenias
Zanubrutinib[4]	160 mg twice daily or 320 mg once daily	Capsules	Reduce zanubrutinib dose to 80 mg once daily	Reduce zanubrutinib dose to 80 mg twice daily	Avoid use	No dosage adjustment recommended	Monitor for arrhythmias, infections, bleeding, and cytopenias

Non-Covalent BTK Inhibitor

Pirtobrutinib[5] **(Based on Approved MCL Labeling)**	200 mg once daily is approved for MCL and is in phase 3 testing in CLL/SLL	Tablets	Avoid use; if use is unavoidable, reduce the pirtobrutinib dose to 50 mg	Avoid use; if use is unavoidable, reduce the pirtobrutinib dose to 50 mg	Avoid use; if use is unavoidable, increase the pirtobrutinib dose	No dosage adjustment recommended	Monitor for arrhythmias, infections, bleeding, and cytopenias

Nemtabrutinib is an emerging non-covalent BTK inhibitor currently being assessed in a phase 3 trial in CLL/SLL (BELLWAVE-008 [NCT05624554])[6]

1. Imbruvica (ibrutinib) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/205552s002lbl.pdf. 2. Calquence (acalabrutinib) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/210259s000lbl.pdf. 3. Sharma S et al. ASH 2021. Abstract 4365. 4. Brukinsa (zanubrutinib) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/213217s007lbl.pdf. 5. Jaypirca (pirtobrutinib) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216059Orig1s000Corrected_lbl.pdf. 6. https://clinicaltrials.gov/ct2/show/NCT05624554.

PRACTICE AID

Dosing, Drug–Drug Interactions, and Safety Monitoring With Venetoclax in CLL/SLL

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Venetoclax[1] standard dose in CLL/SLL

- 400 mg once daily with ramp-up dosing to target dose by week 5
- Tablets: 10 mg, 50 mg, and 100 mg

Ramp-Up Dosing Schedule

WEEK 1	WEEK 2	WEEK 3	WEEK 4
20 mg Once daily	50 mg Once daily	100 mg Once daily	200 mg Once daily
			

Strong CYP3A Inhibitors	Moderate CYP3A Inhibitors	Moderate or Strong CYP3A Inducers	P-gp Inhibitors	Safety Warnings
Contraindicated during initiation and ramp-up phase and avoid use during all phases; if use is unavoidable, reduce venetoclax dose by at least 75%	Avoid use; if use is unavoidable, reduce venetoclax dose by at least 50%	Avoid use	Avoid use; if use is unavoidable, reduce venetoclax dose by at least 50%	• Anticipate for TLS: premedicate with antihyperuricemics and ensure adequate hydration • Monitor for neutropenia: check blood counts and for signs of infection • Do not administer live attenuated vaccines prior to, during, or after treatment

1. Venclexta (venetoclax) Prescribing Information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2016/208573s000lbl.pdf.