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Venetoclax (Venclexta®) for the Treatment of Acute Myeloid Leukemia

Description: The purpose of this document is to discuss the approval of venetoclax for acute myeloid leukemia (AML) and the management of select side effects.

Background: Venetoclax is a BCL-2 inhibitor and is indicated for use in:[1,2]

- AML
  - Newly diagnosed AML in adults 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy in combination with azacitidine, or decitabine, or low-dose cytarabine

Most common adverse reactions (≥ 20%):[1]

- Nausea, diarrhea, thrombocytopenia, constipation, neutropenia, febrile neutropenia, fatigue, vomiting, edema, pyrexia, pneumonia, dyspnea, hemorrhage, anemia, rash, abdominal pain, sepsis, musculoskeletal pain, dizziness, cough, oropharyngeal pain, and hypotension

PQI Process:

- Upon receipt of prescription for venetoclax to treat AML, confirm the dosing and ramp-up schedule is appropriate for the indication
- Review concomitant therapies and recommend appropriate dose adjustments if interactions exist
  - Strong or moderate CYP3A inhibitors or a P-gp inhibitors increase venetoclax Cmax and AUC which may increase venetoclax toxicities including the risk of TLS
  - Concomitant use with a strong CYP3A inhibitor at initiation and during the ramp-up phase in patients with CLL/SLL is contraindicated
  - Resume the venetoclax dosage that was used prior to concomitant use with a strong or moderate CYP3A inhibitor or a P-gp inhibitor 2 to 3 days after discontinuation of the inhibitor
  - Avoid grapefruit products, Seville oranges, and starfruit during treatment with venetoclax
- Ensure the WBC < 25 $x10^9$/L prior to starting; if WBC > 25 $x10^9$/L, cytoreduction is recommended prior to starting venetoclax
- For patients with risk factors for TLS, additional measures such as increased laboratory monitoring, hospitalization, antihyperuricemic agents should be considered, as well as decreased starting dose
- TLS labs (including potassium, uric acid, calcium, phosphorus, and creatinine) should be monitored at baseline and 6 to 8 hours after the first dose/each dose increase
  - In select patients, rasburicase may be used for TLS (see TLS Risk Assessment Tool and Use of Rasburicase (Elitek®) for Treatment of Tumor Lysis Syndrome PQI)

Venetoclax Ramp-Up Schedule in AML	
Day 1	100 mg
Day 2	200 mg
Day 3	400 mg
Day 4 and beyond	400 mg with hypomethylating agent or 600 mg with low dose cytarabine

Coadministered Medication	Ramp Up Dose Modification	Steady Daily Dose Modification
Posaconazole	Day 1: 10 mg Day 2: 20 mg Day 3: 50 mg Day 4: 70 mg	70 mg
Other Strong CYP3A4 Inhibitors	Day 1: 10 mg Day 2: 20 mg Day 3: 50 mg Day 4: 100 mg	100 mg
Moderate CYP3A4 Inhibitors and P-gp Inhibitors	At least a 50% dose reduction is advised A modified ramp up schedule can be considered Day 1: 50 mg Day 2: 100 mg Day 3: 200 mg	200 mg

- See Dose Modification Charts for Venetoclax Treatment Tool
- Bone marrow assessment recommended at the end of Cycle 1 to measure response[1,2]
    - After achieving remission, treatment should be delayed until counts recover

Patient-Centered Activities:

- Provide Patient Education Sheet (PES)
    - Do not chew, crush or break tablets
    - Take once daily with food and water
    - Confirm the titration schedule with the patient
- Confirm the patient is on a uric acid lowering agent 2-3 days prior to starting therapy and is staying adequately hydrated
- Review common adverse events like diarrhea, nausea or vomiting, fatigue, and lab abnormalities
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. Venetoclax [package insert]. North Chicago, IL: AbbVie, Inc.; July 2024.
2. NCCN Guidelines: Acute Myeloid Leukemia. Version 2.2025. National Comprehensive Cancer Network; 2025. Accessed July 18, 2025.