Venclexta® (venetoclax) – New indication

- On November 21, 2018, AbbVie and Roche announced the FDA approval of Venclexta (venetoclax), in combination with azacitidine, or decitabine, or low-dose cytarabine (LDAC) for the treatment of newly-diagnosed acute myeloid leukemia (AML) in adults who are age 75 years or older, or who have comorbidities that preclude use of intensive induction chemotherapy.
    - This indication is approved under accelerated approval based on response rates. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.
- Venclexta is also approved for the treatment of adult patients with chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), with or without 17p deletion, who have received at least one prior therapy.
- AML is a rapidly progressing cancer that forms in the bone marrow and results in an increased number of abnormal white blood cells in the bloodstream and bone marrow. AML is the most common type of aggressive leukemia in adults and has the lowest survival rate for all types of leukemia. The American Cancer Society estimates that in 2018, approximately 19,520 people will be diagnosed with AML and approximately 10,670 patients will die of the disease.
- The approval of Venclexta's new indication was based on two open-label non-randomized studies in patients with newly diagnosed AML who were ≥ 75 years of age, or had comorbidities that precluded the use of intensive induction chemotherapy. In study 1, patients received Venclexta in combination with azacitidine (n = 84) or decitabine (n = 31). In study 2, patients received Venclexta in combination with LDAC (n = 82). Efficacy was established based on the rate of complete remission (CR) and the duration of CR. A key secondary endpoint was complete remission with partial hematological recovery (CRh).
    - In study 1, the rate of CR was 37% (95% CI: 26, 50) and the rate of CRh was 24% (95% CI: 14, 36) for those who received Venclexta plus azacitidine. For patients who achieved a CR, the median observed time in remission was 5.5 months (range: 0.4 to 30 months). For those who received Venclexta plus decitabine, the rate of CR was 54% (95% CI: 25, 81) and the rate of CRh was 7.7% (95% CI: 0.2, 36). For patients who achieved a CR, the median observed time in remission was 4.7 months (range: 1.0 to 18 months).
    - In study 2, the rate of CR and CRh was 21% (95% CI: 12, 34) for those who received Venclexta plus LDAC. For patients who achieved a CR, the median observed time in remission was 6.0 months (range: 0.3 to 25 months).
- The most common adverse reactions (≥ 30%) with Venclexta use in combination with azacitidine, decitabine, or LDAC were nausea, diarrhea, thrombocytopenia, constipation, neutropenia, febrile neutropenia, fatigue, vomiting, peripheral edema, pyrexia, pneumonia, dyspnea, hemorrhage, anemia, rash, abdominal pain, sepsis, back pain, myalgia, dizziness, cough, oropharyngeal pain, and hypotension.
- The recommended dose of Venclexta for the treatment of AML depends on the combination agent. Venclexta should be taken orally once daily with a meal and water. Azacitidine or decitabine or LDAC should also be initiated on day 1.

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	Venclexta Daily Dose	
Day 1	100 mg	
Day 2	200 mg	
Day 3	400 mg	
Day 4 and beyond	400 mg when dosing in combination with azacitidine or decitabine	600 mg when dosing in combination with LDAC

  - Venclexta, in combination with azacitidine or decitabine or LDAC, should be continued until disease progression or unacceptable toxicity is observed.
  - Patient-specific factors should be assessed for level of risk of tumor lysis syndrome (TLS) and prophylactic hydration and anti-hyperuricemics should be provided to patients prior to first dose of Venclexta to reduce risk of TLS.
  - Refer to the azacitidine, decitabine, and LDAC drug labels for additional dosing information.

- Refer to the Venclexta drug label for dosing information for treatment of CLL/SLL.