Entresto® (sacubitril/valsartan) – Expanded indication

- On February 16, 2021, Novartis announced the FDA approval of Entresto (sacubitril/valsartan), to reduce the risk of cardiovascular death and hospitalization for heart failure (HF) in *adult patients with chronic heart failure (CHF)*. Benefits are most clearly evident in patients with left ventricular ejection fraction (LVEF) below normal.
    - LVEF is a variable measure, so use clinical judgment in deciding whom to treat.
    - Entresto was previously approved to reduce the risk of cardiovascular death and hospitalization for HF in patients with *CHF (NYHA Class II-IV) and reduced ejection fraction*.
- Entresto is also approved for the treatment of symptomatic HF with systemic left ventricular systolic dysfunction in pediatric patients aged one year and older.
- Approximately 6 million people in the U.S. are living with CHF. Approximately 3 million have reduced ejection fraction, and of the remaining 3 million, about 2 million have preserved ejection fraction HF with LVEF below normal.
    - Entresto is the first approved therapy for both those with HF with reduced ejection fraction and many with HF with preserved ejection fraction.
- The approval of Entresto for the expanded indication was based on the PARAGON-HF trial, a randomized, double-blind study in 4,796 adult patients with symptomatic HF with left ventricular ejection fraction ≥ 45%, and structural heart disease. Patients received either Entresto or valsartan. The primary endpoint was the rate of the composite endpoint of total (first and recurrent) HF hospitalizations and cardiovascular death.
    - Entresto had a numerical reduction in the rate of the composite endpoint (rate ratio [RR] 0.87, 95% CI: 0.75, 1.01; p = 0.06). The event rate was 12.8 and 14.6 for Entresto and valsartan, respectfully.
    - The treatment effect was primarily driven by the reduction in total HF hospitalizations in patients randomized to Entresto (RR 0.85, 95% CI: 0.72, 1.00).
- The recommended starting dose of Entresto for the treatment of adults with HF is 49/51 mg orally twice daily. The dose of Entresto should be doubled after 2 to 4 weeks to the target maintenance dose of 97/103 mg twice daily, as tolerated by the patient.
    - Refer to the Entresto drug label for pediatric dosing.