Zepbound® (tirzepatide) – New indication

- On December 20, 2024, the FDA announced the approval of Eli Lilly's Zepbound (tirzepatide), in combination with a reduced-calorie diet and increased physical activity, for treatment of **moderate to severe obstructive sleep apnea (OSA) in adults with obesity**.

- Zepbound is also approved in combination with a reduced-calorie diet and increased physical activity to reduce excess body weight and maintain weight reduction long term in adults with obesity or adults with overweight in the presence of at least one weight-related comorbid condition.

- OSA is a breathing disorder characterized by complete or partial collapses of the upper airway during sleep, which can lead to pauses in breathing (apnea) or shallow breathing (hypopnea). Some of the key symptoms associated with OSA are fatigue, excessive daytime sleepiness, and disrupted sleep. **OSA is more common in people who have overweight or obesity**.

- Zepbound is the first drug FDA approved for treatment of OSA.

- The approval of Zepbound for the new indication was based on two randomized, double-blind, placebo-controlled studies (Study 5 and 6) in 469 adult patients with moderate to severe OSA (apnea-hypopnea index [AHI] ≥ 15) and with obesity (BMI ≥ 30 kg/m^2). Patients were randomized to receive Zepbound or placebo for 52 weeks. Study 5 included patients who were unable or unwilling to use Positive Airway Pressure (PAP) therapy and Study 6 included patients who were on PAP therapy. The primary endpoint was the change from baseline in the AHI at week 52. AHI is a measurement of how many times a person stops breathing (apnea) or breathes shallowly (hypopnea) per hour during sleep.

    - In Study 5, the change from baseline in AHI at week 52 was -5.3 and -25.3 with placebo and Zepbound, respectively (difference -20, 95% CI: -25.8, -14.2; $p < 0.001$).
    - In Study 6, the change from baseline in AHI at week 52 was -5.5 and -29.3 with placebo and Zepbound, respectively (difference -23.8, 95% CI: -29.6, -17.9; $p < 0.001$).

- Zepbound carries a boxed warning for risk of thyroid C-cell tumors.

- The recommended starting dosage of Zepbound for all indications is 2.5 mg injected subcutaneously once weekly for 4 weeks.

    - The recommended maintenance dosage for OSA is 10 mg or 15 mg injected subcutaneously once weekly.
    - The recommended maintenance dosage for weight reduction is 5 mg, 10 mg, or 15 mg, injected subcutaneously once weekly.