

# Zepbound® (tirzepatide) for Obstructive Sleep Apnea

FACT SHEET FOR SLEEP PHYSICIANS

## What it is:

**Zepbound (tirzepatide)** is a once-weekly GIP/GLP-1 receptor agonist. In December 2024, FDA approved it as the first medication for moderate-to-severe obstructive sleep apnea (OSA) in adults with obesity, to be used with reduced-calorie diet and increased physical activity.

## Indication (OSA)

**Adults with obesity (body-mass index [BMI]  $\geq 30$  kg/m<sup>2</sup>) and moderate-to-severe OSA (apnea-hypopnea index [AHI]  $\geq 15$  events per hour),** adjunct to diet and physical activity. Consider as part of comprehensive OSA care along with positive airway pressure (PAP) therapy, oral appliance therapy, or surgery as appropriate, not as a replacement for PAP. There is no head-to-head evidence to date that compares Zepbound with other OSA treatments.

## Dosing and administration

- Subcutaneously administered weekly
- **Start:** Begin at 2.5 mg weekly  $\times$  4 weeks, then increase by 2.5 mg every  $\geq 4$  weeks based on tolerability/efficacy.
- **OSA maintenance dose:** 10 mg or 15 mg weekly (max 15 mg)
- Use along with diet + physical activity.



## Contraindications

- Personal or family history of medullary thyroid carcinoma (MTC) or multiple endocrine neoplasia syndrome type 2 (MEN 2).
- Serious hypersensitivity to tirzepatide or excipients
- Pregnancy

## Clinical Evidence

SURMOUNT-OSA trial — two parallel trials in adults with obesity and moderate-severe OSA (one with PAP users; one unable/unwilling to use PAP)

### Primary endpoint: change in AHI at Week 52

- **No PAP group:** AHI  $-25.3$  events/h on tirzepatide vs  $-5.3$  with placebo;  $-50.7\%$  vs  $-3.0\%$  change in AHI; 61% achieved  $\geq 50\%$  AHI reduction (vs 19% placebo).
- **PAP group:** AHI  $-29.3$  events/h on tirzepatide vs  $-5.5$  with placebo;  $-58.7\%$  vs  $-2.5\%$  change; 72% achieved  $\geq 50\%$  AHI reduction (vs 23% placebo).

### Remission/mild OSA with symptom resolution (AHI $< 5$ or 5-14 & Epworth Sleepiness Scale [ESS] $\leq 10$ ):

- 42% (No PAP group) and 50% (PAP group) on tirzepatide vs 16% and 14% on placebo.

### Weight & physiologic measures:

- Weight  $\downarrow$   $\sim 18$ -20% vs  $\sim 2\%$  with placebo at Week 52; hypoxic burden and ESS improved more than placebo.



## Key Warnings & Precautions

- **Boxed warning:** There is a risk of thyroid C-cell tumors (observed in rodents; human relevance unknown). Avoid it in MTC/MEN 2.
- **Severe gastrointestinal (GI) adverse reactions:** It is not recommended in severe GI disease including severe gastroparesis. Use caution in patients with issues with GI motility (generally recommended against given the effects on gastric emptying).
- **Acute pancreatitis, gallbladder disease, acute kidney injury from dehydration:** To avoid acute kidney injury from dehydration, patients need to maintain fluids (generally 2L per day). Stop the medication in patients with gallbladder disease or pancreatitis.
- **Hypoglycemia:** There is a risk when used with insulin/secretagogues; consider dose reductions of those agents.
- **Oral contraceptives:** Efficacy may be reduced with dose escalations; use non-oral or add barrier contraceptive methods for 4 weeks after initiation/escalation.
- **Heart failure with reduced ejection fraction (HFrEF):** Use with caution given the findings of the FIGHT and EXSCel trials.

## Common Adverse Effects

Dose-related nausea, diarrhea, vomiting, constipation, abdominal pain/discomfort, injection-site reactions, fatigue, and gastroesophageal reflux disease (GERD)

## Outcomes to Discuss with Patients

- **OSA improvement:** AHI could potentially be reduced by  $\geq 50\%$ , with a higher likelihood of remission/mild OSA with symptom resolution over 52 weeks – vs placebo
- **Substantial weight loss:** Weight loss of ~18–20% at 1 year is a benefit that likely drives OSA improvement; continued weight management is needed to sustain the effect.
- **Complementary treatment:** Many patients will still need PAP and/or other OSA therapies.
- **Maintenance treatment:** Patients likely will experience weight regain if medication is discontinued.

## Quick Workflow Tips

1. **Eligibility:** Adults with BMI  $\geq 30$  kg/m<sup>2</sup> with moderate–severe OSA.

**Contraindications:** history of MTC/MEN 2, GERD and GI motility issues, pancreatitis.

2. **Start & titrate:** Begin at 2.5 mg weekly → escalate every  $\geq 4$  weeks to **10–15 mg** as tolerated; monitor side effects and weight reduction closely; reinforce diet/physical exercise; coordinate with PAP and other OSA treatment plan.

*\*Caution on oral contraceptive pills: A backup method of contraception is needed for at least 4 weeks after starting Zepbound and after any dose increases.*

3. **Monitor:** Monitor weight, AHI/ESS (consider a repeat home sleep apnea test or polysomnogram to reassess once stabilized weight nadir), GI tolerance, gallbladder/pancreatitis symptoms, renal status if volume depleted; adjust diabetes medications.
4. **Follow-up:** Reassess PAP needs as AHI improves along with weight loss; maintain long-term weight plan to sustain OSA benefit.

## References:

### Clinical Trials (SURMOUNT-OSA)

Malhotra A, Grunstein RR, Fietze I, et al. Tirzepatide for the treatment of obstructive sleep apnea and obesity. *N Engl J Med*. 2024;391(13):1193-1205. <https://doi.org/10.1056/nejmoa2404881>

### FDA Press Release

U.S. Food and Drug Administration. FDA approves first medication for obstructive sleep apnea. December 20, 2024. <https://www.fda.gov/news-events/press-announcements/fda-approves-first-medication-obstructive-sleep-apnea>

### U.S. Prescribing Information

Eli Lilly and Company. Zepbound (tirzepatide) injection, for subcutaneous use. Prescribing information. December 2024. <https://zepbound.lilly.com/>

### Label Safety & Warnings

U.S. Food and Drug Administration. Zepbound (tirzepatide). Highlights of prescribing information. Revised February 2025.

### AASM Statement

American Academy of Sleep Medicine. Zepbound approval for sleep apnea: American Academy of Sleep Medicine statement. December 23, 2024. <https://aasm.org/zepbound-approved-fda-first-sleep-apnea-medication/>