



Zepbound (tirzepatide) for the Treatment of Obstructive Sleep Apnea

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Zepbound (tirzepatide) for the Treatment of Obstructive Sleep Apnea	1
Summary	2
Definitions	2
Clinical Indications	3
Medical Necessity Criteria for Initial Clinical Review	3
Initial Indication-Specific Criteria	3
Obstructive Sleep Apnea	3
Medical Necessity Criteria for Subsequent Clinical Review	4
Subsequent Indication-Specific Criteria	4
Obstructive Sleep Apnea	4
Experimental or Investigational / Not Medically Necessary[s]	5
References	5
Appendix	7
Clinical Guideline Revision / History Information	8

Summary

Obstructive sleep apnea (OSA) is a common sleep disorder characterized by repetitive episodes of complete or partial upper airway obstruction during sleep, leading to reduced or absent breathing and sleep fragmentation. OSA is associated with significant morbidity, including excessive daytime sleepiness, impaired cognitive function, and increased risk of cardiovascular disease, metabolic disorders, and accidents.

Obesity is a major risk factor for OSA, and weight loss is an important component of OSA management. However, achieving and maintaining significant weight loss through lifestyle modifications alone can be challenging for many patients.

Zepbound (tirzepatide) is a novel once-weekly injectable medication that acts as a dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist. Initially approved for the treatment of type 2 diabetes and chronic weight management, tirzepatide has shown promising results in reducing body weight and improving metabolic parameters.

- Recent clinical trials have demonstrated that Zepbound (tirzepatide) can significantly reduce the severity of OSA in adults with obesity, as measured by the apnea-hypopnea index (AHI) and other sleep-related parameters. Zepbound (tirzepatide) treatment was associated with improvements in OSA-related symptoms, quality of life, and cardiovascular risk factors.

NOTE: This clinical guideline addresses the use of Zepbound (tirzepatide) for the treatment of moderate-to-severe obstructive sleep apnea in adults with obesity. It does not apply to the use of Zepbound (tirzepatide) for other indications, such as type 2 diabetes management or chronic weight management in patients without OSA. Coverage of Zepbound (tirzepatide) for weight management may vary depending on a member's benefit policy; please refer to the applicable plan documents or contact the Plan to confirm coverage details.

- Please refer to the Plan's Weight Loss Agents (PG070) Clinical Guideline for specific coverage criteria related to the use of Zepbound (tirzepatide) and other GLP-1 receptor agonists for weight management in members without OSA. The Plan's Weight Loss Agents (PG070) Clinical Guideline only applies to members whose Plan covers prescription drugs prescribed for the treatment of obesity or for use in any weight reduction, weight loss, or dietary control.
- Please refer to the Plan's Antidiabetic Agents - Glucagon-like Peptide-1 (GLP-1) Receptor Agonists (PG152) for specific coverage criteria related to the use of GLP-1 RAs in those with Diabetes Mellitus.

Definitions

"Apnea-hypopnea index (AHI)" is the number of apneas and hypopneas per hour of sleep, used to assess the severity of OSA.

Body mass index (BMI)" is a measure of body fat based on height and weight that applies to adult men and women.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"Habitual snoring" is snoring every night or almost every night.

"Moderate obstructive sleep apnea" is defined as an AHI of 15 to 30 events per hour.

"Obesity" is defined as a BMI of 30 kg/m² or greater.

"Obstructive sleep apnea (OSA)" is a sleep disorder characterized by repetitive episodes of complete or partial upper airway obstruction during sleep.

"Severe obstructive sleep apnea" is defined as an AHI greater than 30 events per hour.

"[s]" indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Obstructive Sleep Apnea

The Plan considers Zepbound (tirzepatide) medically necessary when ALL of the following criteria are met:

1. The medication is prescribed by or in consultation with a sleep specialist, pulmonologist, or other physician who regularly treats sleep disorders; *AND*
2. The member is 18 years of age or older; *AND*
3. The member has a diagnosis of moderate-to-severe obstructive sleep apnea (AHI ≥ 15 events per hour) confirmed by polysomnography or home sleep apnea testing; *AND*
4. The member has a body mass index (BMI) ≥ 30 kg/m²; *AND*
5. The member meets ONE (1) of the following^[s]:
 - a. The member is currently using continuous positive airway pressure (CPAP) therapy or other appropriate noninvasive ventilation (e.g., bi-level positive airway pressure [BiPAP],

automatic positive airway pressure [APAP], adaptive servo ventilation [ASV]) and requires additional OSA management; *or*

- b. The member is unable to use, or has tried and failed, or has a contraindication or intolerance to, at least 3 months of CPAP therapy or other appropriate noninvasive ventilation (e.g., BiPAP, APAP, ASV); *AND*
6. The member meets ALL of the following:
 - a. No history of type 1 diabetes (T1DM) or type 2 diabetes mellitus (T2DM); *and/or*
 - b. No personal history of multiple endocrine neoplasia type 2 (MEN2); *and*
 - c. No personal or family history of medullary thyroid carcinoma; *and*
 - d. Not pregnant; *AND*
7. Zepbound (tirzepatide) will be used in combination with:^[5]
 - a. Lifestyle modifications including reduced calorie diet and increased physical activity; *and*
 - b. Standard OSA treatments as appropriate (e.g., CPAP, oral appliances), unless the member is unable to use CPAP; *AND*
8. Zepbound (tirzepatide) will not be used concurrently with other tirzepatide-containing products or any other GLP-1 receptor agonists; *AND*
9. The prescribed dose does not exceed 15 mg once weekly.

If the above prior authorization criteria are met, the requested product will be authorized for up to 6-months.^[5]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Indication-Specific Criteria

Obstructive Sleep Apnea

The Plan considers Zepbound (tirzepatide) medically necessary when ALL of the following criteria are met:

1. The member has demonstrated clinical response as demonstrated by at least ONE (1) of the following:
 - a. A clinically significant reduction in AHI (e.g., $\geq 50\%$ reduction from baseline or AHI < 15 events per hour) as compared to baseline (i.e., pre-treatment); *or*
 - b. Improvement in OSA-related symptoms (e.g., daytime sleepiness, habitual snoring, morning headaches); *AND*
2. The member continues to adhere to lifestyle modifications; *AND*
3. If the member has achieved remission or non-symptomatic OSA, the prescriber provides rationale for continuing therapy (e.g., at risk for returning symptoms); *AND*
4. The member has not developed any contraindications to continue Zepbound (tirzepatide) therapy; *AND*

5. The member is not receiving other tirzepatide-containing products or any other GLP-1 receptor agonists; *AND*
6. The prescribed dose is 10 mg or 15 mg once weekly.

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.^[5]

Experimental or Investigational / Not Medically Necessary^[5]

Zepbound (tirzepatide) is considered experimental, investigational, or not medically necessary for all other indications, including but not limited to[†], the following:

- Treatment of mild OSA (AHI < 15 events per hour). The pivotal trial which resulted in approval of Zepbound (tirzepatide) for the management of OSA did not include those with mild OSA. Participants had to have moderate-to-severe OSA defined by having AHI ≥15 events/hour.
- Treatment of OSA in non-obese individuals (BMI < 30 kg/m²). Only those with a BMI of ≥30 kg/m² were included in the pivotal trial; it is unclear if those with lower BMI and thus considered to be non-obese, would benefit from Zepbound (tirzepatide) for the management of OSA.
- Treatment of central sleep apnea. Zepbound (tirzepatide) has not been studied for the management of central sleep apnea. Those with central or mixed sleep apnea were excluded from the pivotal trial.
- Treatment of obesity without concurrent OSA. Please refer to the Plan's coverage policy for weight loss agents, PG070 - Weight Loss Agents.
- Treatment of type 2 diabetes without concurrent OSA. The pivotal trial for Zepbound (tirzepatide) explicitly excluded those with a history of type 1 or 2 diabetes mellitus, ketoacidosis, or hyperosmolar state/coma, or those with a hemoglobin A1c of ≥6.5% at baseline.

†The above list of experimental and investigational uses is not exhaustive. The fact that an indication is not listed above does not imply that Zepbound (tirzepatide) is medically necessary for that use. All requests for Zepbound (tirzepatide) for non-FDA approved indications will be reviewed on an individual basis in accordance with the member's benefit policy and applicable Clinical Guidelines.

NOTE: While the clinical evidence supports the medical necessity of Zepbound (tirzepatide) for weight management in obese and some overweight individuals with or without OSA, as outlined in Pharmacy Guideline - Weight Loss Agents (PG070), coverage depends on the specific terms of the member's benefit plan. Members should refer to their specific plan documents or contact the Plan to confirm coverage details for weight loss medications.

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Appendix

In the SURMOUNT-OSA trials [ClinicalTrials.gov Identifier: NCT05412004], Zepbound (tirzepatide) demonstrated significant reductions in AHI and improvements in OSA-related outcomes in adults with obesity and moderate-to-severe OSA. Key findings include:

- Mean reduction in AHI of up to 29.3 events per hour (58.7% change from baseline) with Zepbound (tirzepatide) compared to 5.5 events per hour with placebo.
- Up to 51.5% of participants treated with Zepbound (tirzepatide) achieved disease resolution (defined as AHI < 5 events/hour or AHI 5-14 events/hour with Epworth Sleepiness Scale score ≤ 10).
- Significant improvements in hypoxic burden, sleep-related quality of life measures, and cardiovascular risk factors (e.g., blood pressure, hsCRP).
- Mean weight loss of 17.7% to 19.6% with Zepbound (tirzepatide) compared to 1.6% to 2.3% with placebo
- Most common adverse events were gastrointestinal and generally mild to moderate in severity.

Table 1: SURMOUNT-OSA Trials - Key Details, Results, and Insights

Aspect	Details
Trial name	SURMOUNT-OSA (Trial 1 and Trial 2) [ClinicalTrials.gov Identifier: NCT05412004]
Intervention	Tirzepatide (maximum tolerated dose of 10 mg or 15 mg) vs placebo, once weekly for 52 weeks.
Study population	469 adults with moderate-to-severe obstructive sleep apnea (OSA) and obesity (Trial 1: 234; Trial 2: 235)
<ul style="list-style-type: none"> • Inclusion criteria 	<ul style="list-style-type: none"> • Age ≥18 years • AHI ≥15 events/hour • Obesity (BMI ≥30) or overweight (BMI ≥27 in Japan) • Trial 1: Unable/unwilling to use PAP therapy • Trial 2: Using PAP therapy for ≥3 months
Exclusion criteria	<ul style="list-style-type: none"> • Type 1 or 2 diabetes • Weight change >5 kg in 3 months before screening • Planned surgery for sleep apnea or obesity • Central or mixed sleep apnea • Major craniofacial abnormalities

Study design	Two phase 3, multicenter, parallel-group, double-blind, randomized, controlled trials.
Number of sites	60 sites across 9 countries
Primary endpoint	Change in AHI from baseline to week 52
Key secondary endpoints	<ul style="list-style-type: none"> ● Percent change in AHI ● Proportion with ≥50% reduction in AHI ● Proportion with AHI <5 or AHI 5-14 with ESS ≤10 ● Percent change in body weight ● Change in hsCRP, hypoxic burden, PROMIS scores, systolic blood pressure
Primary endpoint results	<ul style="list-style-type: none"> ● Trial 1: -20.0 events/hour difference (95% CI -25.8 to -14.2), p<0.001 <ul style="list-style-type: none"> ○ Tirzepatide, -25.3 events/hr vs Placebo, -5.3 events ● Trial 2: -23.8 events/hour difference (95% CI -29.6 to -17.9), p<0.001 <ul style="list-style-type: none"> ○ Tirzepatide, -29.3 events/hr vs Placebo, -5.5 events/hr
Key secondary endpoint results	<p>Significant improvements in all key secondary endpoints with tirzepatide vs placebo</p> <ul style="list-style-type: none"> ● Weight loss: 17.7% vs 1.6% (Trial 1), 19.6% vs 2.3% (Trial 2) ● Significant reductions in hypoxic burden and hsCRP ● Improved sleep-related patient-reported outcomes
Adverse events	<ul style="list-style-type: none"> ● Most common adverse events were gastrointestinal (mild to moderate) ● Serious AEs were similar between groups. No deaths reported ● Two cases of acute pancreatitis in tirzepatide group (Trial 2)
Conclusions	<p>Tirzepatide significantly reduced AHI, body weight, hypoxic burden, hsCRP, blood pressure, and improved sleep-related patient-reported outcomes in adults with moderate-to-severe OSA and obesity.</p> <p><i>Note: The results from both trials demonstrated consistent efficacy regardless of baseline PAP therapy status, suggesting potential benefit for patients both with and without concurrent PAP use.</i></p>

AHI = apnea-hypopnea index, BMI = body mass index, PAP = positive airway pressure, ESS = Epworth Sleepiness Scale, hsCRP = high-sensitivity C-reactive protein, PROMIS = Patient-Reported Outcomes Measurement Information System, CI = confidence interval, AEs = adverse events

[Clinical Guideline Revision / History Information](#)

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