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Policy Number: C29112-A

Zepbound (tirzepatide) NC

PRODUCTS AFFECTED

Zepbound (tirzepatide)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Overweight/obesity, Obstructive sleep apnea

REQUIRED MEDICAL INFORMATION:
In states where weight loss drugs are a benefit exclusion, Zepbound (tirzepatide) is considered a benefit exclusion for all indications, including but not limited to weight reduction and chronic weight management, weight reduction to treat moderate to severe obstructive sleep apnea, and so on.

Weight loss drugs are benefit exclusions as outlined in the Marketplace Evidence of Coverage.
MOLINA REVIEWER NOTE: For California Marketplace and New Mexico Marketplace, please see Appendix.

Zepbound (tirzepatide) is excluded from coverage for overweight/obesity per Social Security 1927 (d)(3)(A).
A State may exclude or otherwise restrict coverage of a covered outpatient drug if the drug is contained in the list:

- **Agents when used for anorexia, weight loss, or weight gain.**
- Agents when used to promote fertility.
- Agents when used for cosmetic purposes or hair growth.

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- Agents when used for the symptomatic relief of cough and colds.
- Agents when used to promote smoking cessation.
- Prescription vitamins and mineral products, except prenatal vitamins and fluoride preparations.
- Nonprescription drugs, except, in the case of pregnant women when recommended in accordance with the Guideline referred to in section 1905(bb)(2)(A), agents approved by the Food and Drug Administration under the over-the-counter monograph process for purposes of promoting, and when used to promote, tobacco cessation.
- Covered outpatient drugs which the manufacturer seeks to require as a condition of sale that associated tests or monitoring services be purchased exclusively from the manufacturer or its designee.
- Barbiturates.
- Benzodiazepines.
- Agents when used for the treatment of sexual or erectile dysfunction, unless such agents are used to treat a condition, other than sexual or erectile dysfunction, for which the agents have been approved by the Food and Drug Administration.

CONTINUATION OF THERAPY:
N/A

DURATION OF APPROVAL:
N/A

PRESCRIBER REQUIREMENTS:
N/A

AGE RESTRICTIONS:
N/A

QUANTITY:
N/A

PLACE OF ADMINISTRATION:
N/A

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Anti-Obesity - GIP & GLP-1 Receptor Agonists

FDA-APPROVED USES:
Indicated 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
- to treat moderate to severe obstructive sleep apnea (OSA) in adults with obesity

Limitations of Use: Coadministration with other tirzepatide-containing products or with any GLP-1 receptor agonist is not recommended.

COMPENDIAL APPROVED OFF-LABELED USES:
None

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APPENDIX

Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*

State Specific Information
State Marketplace
California (Source: California Title 28)
"(e) Exclusions
Plans that provide coverage for outpatient prescription drug benefits are not required to provide coverage for prescription drugs that meet the following conditions:…
(3) When prescribed solely for the purposes of losing weight, *except when medically necessary for the treatment of morbid obesity*. Plans may require enrollees who are prescribed drugs for morbid obesity to be enrolled in a comprehensive weight loss program, if covered by the plan, for a reasonable period of time prior to or concurrent with receiving the prescription drug."
See Weight Management Therapy CA MMKP C28425-A.

New Mexico (Source: New Mexico)
"Weight Loss Programs: Covered: Dietary evaluations and counseling for the medical management of morbid obesity and obesity. *Prescription drugs medically necessary for the treatment of obesity and morbid obesity are also covered.* See also, benefits described under Bariatric Surgery. Not Covered: The following are not covered: Treatments and medications for the purpose of weight reduction or control, except for medically necessary treatment of morbid obesity and obesity. Exercise equipment, videos, personal trainers, club members and weight reduction programs."
Phendimetrazine and phentermine are on formulary.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Zepbound (tirzepatide) is a dual glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist that is approved to reduce excess body weight and maintain weight reduction in patient with obesity or who are overweight with a weight-related comorbidity. It is also approved in combination with a reduced-calorie diet and increased physical activity, for adults with moderate to severe obstructive sleep apnea (OSA) and obesity.

Obstructive sleep apnea is a chronic disorder characterized by respiratory events (hypopneas and apneas) during sleep. Risk factors include older age, male gender, postmenopausal women, airway and facial abnormalities, and obesity. Obesity has a strong correlation to the development of OSA. An obvious result of OSA is daytime sleepiness, but patients with OSA are at risk for more severe disorders such as cardiovascular disease and metabolic dysfunction. Diagnosis is confirmed by polysomnography and classified based on the apnea-hypopnea index (AHI). Mild to severe is based on the number of respiratory events per hour of sleep – the more events, the greater the severity.

Treatment of OSA includes reducing modifiable risk factors, such as obesity through weight loss, and avoidance of sedatives. If a patient has moderate or severe disease, use of positive airway pressure (PAP) is recommended. PAP therapy consists of a mask worn during sleep that administers pressurized air into the airway in order to keep it open. Clinical practice guidelines from the American Academy of Sleep Medicine recognize that OSA is a chronic disease that rarely resolves without substantial weight loss or corrective surgery. The assumed mechanism by which Zepbound exerts a positive impact on patients with OSA is through weight loss.

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The efficacy and safety of Zepbound for OSA in patients with obesity was evaluated in a master protocol clinical trial (NCT05412004) that included two randomized, double-blind, placebo-controlled trials (Study 5 and Study 6) of 52 weeks duration. The two trials enrolled a total of 469 adult patients. Patients with type 2 diabetes mellitus were excluded and all patients received instruction on a reduced-calorie diet and increased physical activity counseling throughout the study. Study 5 enrolled adult patients who were unable or unwilling to use Positive Airway Pressure (PAP) therapy. Study 6 enrolled adult patients who were on PAP therapy. The primary endpoint for Studies 5 and 6 was the change from baseline in the apnea-hypopnea index (AHI) at Week 52. In Studies 5 and 6, treatment with Zepbound for 52 weeks resulted in a statistically significant reduction in AHI compared with placebo, and greater proportions of patients treated with Zepbound achieved remission or mild non-symptomatic OSA compared to placebo. In both Studies 5 and 6, patients treated with Zepbound achieved a greater reduction in systolic blood pressure and high-sensitivity C-reactive protein levels compared to placebo. Patients also showed improvement in sleep-related impairment compared to those who received placebo. Sleep-related impairment was assessed using the Patient-Reported Outcomes Measurement Information System (PROMIS) Short Form Sleep-Related Impairment 8a.

The adverse event profile in the OSA trials was consistent with previously published studies. The most common adverse events are gastrointestinal in nature.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
Contraindications to Zepbound (tirzepatide) include: personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2, known serious hypersensitivity to tirzepatide or any of the excipients in Zepbound, avoid Zepbound in patients with a history of suicidal attempts or active suicidal ideation.

OTHER SPECIAL CONSIDERATIONS:
Zepbound (tirzepatide) has a Black Box Warning for risk of thyroid C-cell tumors. In rats, tirzepatide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether Zepbound causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of tirzepatide-induced rodent thyroid C-cell tumors has not been determined. Zepbound is contraindicated in patients with a personal or family history of MTC or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of Zepbound and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with Zepbound.

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover*

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claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Zepbound SOLN 2.5MG/0.5ML single-dose vial
Zepbound SOLN 5MG/0.5ML single-dose vial
Zepbound SOAJ 2.5MG/0.5ML single-dose pen
Zepbound SOAJ 5MG/0.5ML single-dose pen
Zepbound SOAJ 7.5MG/0.5ML single-dose pen
Zepbound SOAJ 10MG/0.5ML single-dose pen
Zepbound SOAJ 12.5MG/0.5ML single-dose pen
Zepbound SOAJ 15MG/0.5ML single-dose pen

REFERENCES

1. Zepbound (tirzepatide) Injection, for subcutaneous use [prescribing information]. Indianapolis, IN: Lilly USA, LLC; December 2024.
2. Patil, S. P., Ayappa, I. A., Caples, S. M., Kimoff, R. J., Patel, S. R., & Harrod, C. G. (2019). Treatment of Adult Obstructive Sleep Apnea with Positive Airway Pressure: An American Academy of Sleep Medicine Clinical Practice Guideline. *Journal of Clinical Sleep Medicine*, *15*(02), 335–343. https://doi.org/10.5664/jcsm.7640
3. Hudgel, D. W., Patel, S. R., Ahasic, A. M., Bartlett, S. J., Bessesen, D. H., Coaker, M. A., … Wilson, K. C. (2018). The Role of Weight Management in the Treatment of Adult Obstructive Sleep Apnea. An Official American Thoracic Society Clinical Practice Guideline. American Journal of Respiratory and Critical Care Medicine, 198(6), e70–e87. https://doi.org/10.1164/rccm.201807-1326st

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q1 2025

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