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Policy Number: C29111-A

Zepbound (tirzepatide) MNR

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:
Obstructive sleep apnea

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. OBSTRUCTIVE SLEEP APNEA:
   1. Documented diagnosis of obstructive sleep apnea
      AND

2. Documentation disorder is moderate to severe as evidenced by an apnea-hypopnea index (AHI) ≥ 15 measured on polysomnography at the time of diagnosis
   AND
3. Documentation member's BMI is 30 kg/m2 or greater
   AND
4. Member has previously attempted weight loss through dietary changes
   AND
5. Documentation that Zepbound (tirzepatide) will be used in combination with a reduced-calorie diet and increased physical activity
   AND
6. Documentation member has failed to achieve therapeutic goals on positive airway pressure (PAP) therapy and use of oral appliances OR those treatments are not able to be used
   AND
7. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal
   AND
8. Documentation member does NOT have a diagnosis of Type 1 or Type 2 diabetes
   AND
9. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [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, when pregnancy is recognized discontinue Zepbound.]

B. OVERWEIGHT/OBESITY:

MOLINA REVIEWER NOTE: PLEASE FIRST REFER TO STATE AND LINE OF BUSINESS EXPLANATION OF BENEFITS TO DETERMINE IF WEIGHT LOSS IS A COVERED BENEFIT.

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.
- 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:

A. OBSTRUCTIVE SLEEP APNEA:

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms
   AND
4. Documentation member does NOT have a diagnosis of Type 1 or Type 2 diabetes

B. OVERWEIGHT/OBESITY: N/A

DURATION OF APPROVAL:
Initial authorization: 6 months, Continuation of Therapy: 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified pulmonologist or sleep medicine specialist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
10mg or 15mg once weekly
Maximum Quantity Limits – 4 pens per 28 days

PLACE OF ADMINISTRATION:
The recommendation is that injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

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

APPENDIX

APPENDIX:
None

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.

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:
All other uses of Zepbound (tirzepatide) are considered experimental/investigational. 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, when pregnancy is recognized discontinue Zepbound.

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 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, 5MG/0.5ML, 7.5MG/0.5ML, 10MG/0.5ML, 12.5MG/0.5ML, 15MG/0.5ML single-dose vial
Zepbound SOAJ 2.5MG/0.5ML, 5MG/0.5ML, 7.5MG/0.5ML, 10MG/0.5ML, 12.5MG/0.5ML, 15MG/0.5ML single-dose pen

REFERENCES

1. Zepbound (tirzepatide) Injection, for subcutaneous use [prescribing information]. Indianapolis, IN: Lilly USA, LLC; April 2025.
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.

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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
REVISION- Notable revisions: Required Medical Information Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q4 2025
NEW CRITERIA CREATION	Q1 2025