# Clinical Policy: Tirzepatide (Zepbound)

Reference Number: NE.PMN.298
Effective Date: 7.1.25
Last Review Date: 6.1.25
Line of Business: Medicaid

Coding Implications
Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

**Description**
Tirzepatide (Zepbound®) is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist.

**FDA Approved Indication(s)**
Zepbound is 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

Limitation(s) of use: Coadministration with other tirzepatide-containing products or any GLP-1 receptor agonist is not recommended.

**Policy/Criteria**
*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of Nebraska Total Care that Zepbound is **medically necessary** when the following criteria are met:

**I. Initial Approval Criteria**

**A. Obstructive Sleep Apnea** (must meet all)**:**

1. Diagnosis of moderate to severe OSA with polysomnography (PSG) evidence of one of the following (a, b, or c):
   a. Apnea-Hypopnea Index (AHI) ≥ 15 respiratory events per hour;
   b. Respiratory Disturbance Index (RDI) ≥ 15;
   c. Respiratory Event Index (REI) ≥ 15;
2. Medication is prescribed by or in consultation with a sleep specialist;
3. Age ≥ 18 years;
4. Body mass index (BMI) ≥ 30 kg/m$^2$;
5. The member has completed a weight management program medically supervised by a physician, nurse practitioner, or physician assistant and counseling for at least 6 months that includes all of the following (a, b, c, d and e):
   a. Behavioral modification;
   b. Reduced calorie diet;
   c. Increased physical activity;

   d. Counseling to avoid sleeping in the supine position;
   e. Counseling to avoid alcohol and sedatives before bedtime
6. The provider attests that the member is currently on and will continue (must meet all):
   a. Behavioral modification;
   b. Reduced calorie diet;
   c. Increased physical activity, if possible;
   d. Compliance with sleep positioning;
   e. Compliance with no alcohol or sedatives before bedtime;
   f. Adherence to the prescribed PAP treatment (defined as > 4 hours of use per night for> 70 percent of nights for 2 or more months) or oral appliance treatment as applicable;
7. Member does not have the following (a and b);
   a. Diagnosis of diabetes mellitus;
   b. HgA1c ≥ 6.5%;
8. Member meets one of the following (a or b or c):
   a. Failure to achieve therapeutic goals on positive airway pressure (PAP) treatment and oral appliance treatment despite optimization of these treatments;
   b. Intolerance to both PAP treatment and oral appliance treatment;
   c. Is not a candidate for both PAP treatment and oral appliance treatment;
9. The member does not have any of the following (a, b and c):
   a. Planned surgery for sleep apnea or obesity
   b. Significant craniofacial abnormalities
   c. A diagnosis of central or mixed sleep apnea
10. The provider attests that the member does not have any of the following (must meet all):
   a. NYHA Class IV Heart failure;
   b. Impaired renal function (eGFR < 30 mL/min/1.73m$^2$);
   c. History of chronic pancreatitis or presence of acute or chronic pancreatitis;
   d. Personal or first-degree relative(s) history of multiple endocrine neoplasia type 2 or medullary thyroid carcinoma;
   e. Known or suspected hypersensitivity to the product;
   f. History of suicidal attempts or active suicidal ideation;
   g. Pregnant, breastfeeding, or intends to become pregnant, or is of childbearing potential and not using a highly effective contraceptive method;
11. Zepbound is not prescribed concurrently with other tirzepatide-containing products or any other GLP-1 receptor agonist(s) or DPP-4 inhibitors;
12. Dose does not exceed the following:
   a. Week 1 through 4: 2.5 mg once weekly;
   b. Week 5 through 8: 5 mg once weekly;
   c. Week 9 through 12: 7.5 mg once weekly;
   d. Week 13 through 16: 10 mg once weekly;
   e. Week 17 through 20: 12.5 mg once weekly;
   f. Week 21 through 24: 15 mg once weekly;
   g. One pen or vial per week.

**Approval duration: 6 months**

**B. Weight Management**

1. Use of Zepbound for the treatment of weight management is a benefit exclusion and will not be authorized.

**Approval duration: Not applicable**

## II. Continued Therapy

**A. Obstructive Sleep Apnea** (must meet all)**:**

1. Member is currently receiving medication via Nebraska Total Care Medicaid benefit or member has previously met initial approval criteria;
2. Medication is prescribed by or in consultation with a sleep specialist;
3. Member is responding positively to therapy as evidenced by one of the following (a, b, or c):
   a. AHI reduction from baseline;
   b. RDI reduction from baseline;
   c. REI reduction from baseline;
4. Member does not have the following (a and b);
   a. Diagnosis of diabetes mellitus
   b. HgA1c ≥ 6.5%
5. Zepbound is not prescribed concurrently with other tirzepatide-containing products or any other GLP-1 receptor agonist(s) or DPP-4 inhibitors;
6. The provider attests that the member is currently on and will continue (must meet all):
   a. Behavioral modification;
   b. Reduced calorie diet;
   c. Increased physical activity;
   d. Compliance with sleep positioning;
   e. Compliance with no alcohol or sedatives before bedtime;
   f. Adherence to the prescribed PAP treatment (defined as > 4 hours of use per night for> 70 percent of nights for 2 or more months) or oral appliance treatment as applicable;
7. The provider attests that the member does not have any of the following (must meet all):
   a. NYHA Class IV Heart failure;
   b. Impaired renal function (eGFR < 30 mL/min/1.73m$^2$);
   c. History of chronic pancreatitis or presence of acute or chronic pancreatitis;
   d. Personal or first-degree relative(s) history of multiple endocrine neoplasia type 2 or medullary thyroid carcinoma (MTC);
   e. Known or suspected hypersensitivity to the product;
   f. History of suicidal attempts or active suicidal ideation;
   g. Pregnant, breastfeeding, or intends to become pregnant, or is of childbearing potential and not using a highly effective contraceptive method;
8. Request meets all the following (a, b, and c):
   a. Dose does not exceed 15 mg once weekly;
   b. After the initial dose escalation period (*see Section V*), maintenance dose is ≥ 10 mg once weekly;
   c. Requested quantity does not exceed one pen or vial per week.

**Approval duration: 12 months**

**B. Weight Management**

1. Use of Zepbound for the treatment of weight management is a benefit exclusion and will not be authorized.

**Approval duration: Not applicable**

## III. Diagnoses/Indications for which coverage is NOT authorized:

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy CP.PMN.53 or evidence of coverage documents.

## IV. Appendices/General Information

*Appendix A: Abbreviation/Acronym Key*

AHI: apnea-hypopnea index
BMI: body mass index
DPP-4: dipeptidyl peptidase-4
eGFR: estimated glomerular filtration rate
FDA: Food and Drug Administration
GIP: glucose-dependent insulinotropic polypeptide
GLP-1: glucagon-like peptide-1
HgA1c: hemoglobin A1c
MTC: medullary thyroid carcinoma
NYHA: New York Heart Association
OSA: obstructive sleep apnea
PAP: positive airway pressure
PSG: polysomnography
RDI: respiratory disturbance index
REI: respiratory event index

*Appendix B: Therapeutic Alternatives*

Not applicable

*Appendix C: Contraindications/Boxed Warnings*

- Contraindication(s): personal or family history of medullary thyroid carcinoma (MTC) or in patients with multiple endocrine neoplasia syndrome type 2 (MEN 2), known serious hypersensitivity to tirzepatide or to any of the excipients in Zepbound
- Boxed warning(s): risk of thyroid C-cell tumors

*Appendix D: General Information*

- BMI = 703 x [weight (lbs)/height (inches)$^2$]
- The American Academy of Sleep Medicine (AASM) classifies the severity of OSA based on polysomnography-derived AHI cutoffs:
  - Mild: ≥ 5 to < 15 events per hour
  - Moderate: ≥ 15 to < 30 events per hour
  - Severe: ≥ 30 events per hour
- The American Thoracic Society practice guidelines recommends that patients with OSA who are overweight or obese be treated with comprehensive lifestyle intervention consisting of 1) a reduced-calorie diet, 2) exercise or increased physical activity, and 3) behavioral guidance.
- The American Association of Clinical Endocrinologists and American College of Endocrinology practice guidelines also recommends patients with OSA who are

overweight or obese be treated with weight-loss therapy including lifestyle intervention and additional modalities as needed. The weight loss goal should be at least 7 or 11% or more.

## V. Dosage and Administration

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| OSA | The recommended starting dosage is 2.5 mg SC once weekly for 4 weeks and increased by 2.5 mg every 4 weeks until the maximum tolerated recommended maintenance dose of 10 mg or 15 mg is achieved | 15 mg/week |

## VI. Product Availability

- Pre-filled, single-dose pens: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg
- Pre-filled, single-dose vials: 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, 15 mg

## VII. References

1. Zepbound Prescribing Information. Indianapolis, IN: Lilly USA, LLC; December 2024. Available at: https://uspl.lilly.com/zepbound/zepbound.html#pi. Accessed January 15, 2024.
2. Malhotra A, Grunstein RR, Fietze I, et al. Tirzepatide for the treatment of obstructive sleep apnea and obesity. NEJM. 2024 Jun 21. doi: 10.1056/NEJMoa2404881. Epub ahead of print.
3. Clinicaltrials.gov. Obstructive sleep apnea master protocol GPIF: A study of tirzepatide (LY3298176) in participants with obstructive sleep apnea (SURMOUNT-OSA). Available at: https://clinicaltrials.gov/study/NCT05412004. Accessed September 12, 2024.
4. Epstein LJ, Kristo D, Strollo PJ, et al. Adult obstructive sleep apnea task force of the American Academy of Sleep Medicine: Clinical guideline for the evaluation, management, and long-term care of obstructive sleep apnea in adults. Journal of Clinical Sleep Medicine 2009. 5(3): 263-276.
5. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: An American Academy of Sleep Medicine Clinical Practice Guideline. Journal of Clinical Sleep Medicine 2017. 13(3):479-504.
6. Patil SP, Ayappa IA, Caples SM, et al. Treatment of adult obstructive sleep apnea with positive airway pressure: An American Academy of Sleep Medicine Clinical Practice Guideline. Journal of Clinical Sleep Medicine 2019. 15(2): 335-343.
7. Mediano O, Gonzalez Mangado N, Montserrat JM, et al. [Translated article] International consensus document on obstructive sleep apnea. Archivos de Bronconeumologia 2022. 58:T52-T68.
8. Hudgel DW, Patel SR, Ahasic AM, et al; The role of weight management in the treatment of adult obstructive sleep apnea. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 2018 Sep 15;198(6):e70-e87.
9. Garvey WT, Mechanick JI, Brett EM, et al. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. Endocr Pract 2016;22:Suppl 3:1-203.

**Coding Implications**
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

| HCPCS Codes | Description |
|---|---|
| C9399 | Unclassified drugs or biologicals |
| J3490 | Unclassified drugs |

| Reviews, Revisions, and Approvals | Date |
|---|---|
| Policy created | 6.4.25 |

**Important Reminder**
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

**Note:**
**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.