Clinical Policy: Tirzepatide (Zepbound)

Reference Number: HNCA.CP.CPA.359
Effective Date: 09.01.24
Last Review Date: 07.24
Line of Business: Commercial

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 as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:

- 30 kg/m^2 or greater (obesity) or
- 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes mellitus, obstructive sleep apnea or cardiovascular disease).

Limitation(s) of use:

- Coadministration with other tirzepatide-containing products or any GLP-1 receptor agonist is not recommended.
- The safety and efficacy of coadministration with other products for weight management have not been established.
- Zepbound has not been studied in patients with a history of pancreatitis.

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, including active participation in an approved weight loss program for at least 6 months prior to use of GLP-1 agonist, which includes a reduced calorie diet, increased physical activity, and behavioral modification.

Note: Not every Group has obesity coverage. If no coverage, but medically necessary, the copayment will be 50% of the prescription cost.

It is the policy of health plans affiliated with Health Net of California that Zepbound is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Weight Management (must meet all)**:**

1. Member meets one of the following (a, b, or c):
   a. BMI ≥ 30 kg/m^2;
   b. BMI ≥ 27 kg/m^2 with at least one indicator of increased cardiovascular risk (e.g., coronary artery/heart disease, hypertension, dyslipidemia, diabetes,

elevated waist circumference) or other obesity-related medical condition (e.g., sleep apnea);

2. Age ≥ 18 years;
3. Zepbound is not prescribed concurrently with other tirzepatide-containing products or any other GLP-1 receptor agonist(s);
4. Documentation supports member's participation in a Health Net approved weight loss program (e.g., Weight Watchers) or other weight loss programs recommended by the prescriber that involves a reduced calorie diet, increased physical activity, and behavioral modification that meets both of the following (a and b):
   a. Been actively enrolled in a Health Net approved weight loss program (e.g., Weight Watchers) or other weight loss programs recommended by the prescriber for at least 6 months prior to use of GLP-1 agonist;
   b. Will continue to be actively enrolled in a weight loss program while concomitantly using Zepbound;
5. Documentation of member's baseline and current height and body weight within the last 30 days;
6. Follow-up visits are planned every 4 months to assess adherence and response to the treatment plan;
7. 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: 16 weeks

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial or health insurance marketplace), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial; or
   b. For drugs NOT on the formulary (commercialor health insurance marketplace), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial.

II. Continued Therapy

A. Weight Management (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. If this is the first renewal request, member has lost ≥ 5% of baseline body weight;
   b. If this is a second or subsequent renewal request, member has lost weight and/or maintained weight loss on therapy;
3. Documentation of member's current height and body weight within the last 30 days;
4. Follow-up visits are planned every 4 months to assess adherence and response to the treatment plan;
5. Zepbound is not prescribed concurrently with other tirzepatide-containing products or any other GLP-1 receptor agonist(s);
6. Documentation that member is actively enrolled in an approved weight loss program that involves a reduced calorie diet, increased physical activity, and behavioral modification adjunct to therapy;
7. 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 ≥ 5 mg once weekly;
   c. Requested quantity does not exceed one pen or vial per week.

Approval duration: 16 weeks

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial or health insurance marketplace), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial; or
   b. For drugs NOT on the formulary (commercial or health insurance marketplace), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial.

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.CPA.09 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A. Abbreviation/Acronym Key

BMI: body mass index
FDA: Food and Drug Administration
GIP: glucose-dependent insulinotropic polypeptide
GLP-1: glucagon-like peptide-1

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 – Weight Management

- BMI = 703 x [weight (lbs)/height (inches)^2].
- Examples of coronary artery/heart disease include coronary artery bypass graft, angina, and history of myocardial infarction or stroke.
- The Endocrine Society practice guideline on pharmacological management of obesity states that a weight loss < 5% after 3 months of therapy indicates the weight loss medication is ineffective. In such cases, the Endocrine Society recommends that the medication be discontinued and alternative medications be considered.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Weight management	The recommended starting dosage is 2.5 mg SC once weekly. The 2.5 mg dosage is for treatment initiation and is not intended for chronic weight management. After 4 weeks, increase the dosage to 5 mg SC once weekly. The dosage may be increased in 2.5 mg increments, after at least 4 weeks on the current dose. The recommended maintenance dosages are	15 mg/week

	5 mg, 10 mg, or 15 mg SC once weekly. Consider treatment response and tolerability when selecting the maintenance dosage. If patients do not tolerate a maintenance dosage, consider a lower maintenance dosage.	

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; March 2024. Available at: https://uspl.lilly.com/zepbound/zepbound.html#pi. Accessed April 11, 2024.
2. Jastreboff AM, Aronne LJ, Ahmad NN, et al.; SURMOUNT-1 Investigators. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med. 2022 Jul 21;387(3):205-216.
3. Garvey WT, Frias JP, Jastreboff AM, et al.; SURMOUNT-2 investigators. Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet. 2023 Aug 19;402(10402):613-626.
4. Hampl SE, Hassink SG, Skinner AC, et al. Clinical practice guideline for the evaluation and treatment of children and adolescents with obesity [published online ahead of print, 2023 Jan 9]. Pediatrics. 2023;e2022060640.
5. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. Circulation. 2014; 129 (suppl 2): S102–S138.
6. Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2015; 100(2): 42362.

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	P&T Approval Date
RT4: Policy created. For documentation of weight loss program, added members has been actively enrolled for at least 6 months, added a weight loss program that also involves behavioral modification, clarified weight loss program to be either a Health Net approved weight loss program or a weight loss program recommended by the prescriber.	12.12.23	02.24
RT4: added newly approved single dose vial formulation; added requirement for documentation of baseline body and current body weight in kg to initial and continued criteria, respectively.	04.11.24	
New CA policy - Added documentation is required that shows member has been enrolled in a weight loss program for at least 6 months prior to use of GLP-1. - Documentation of baseline and current height and weight within the last 30 days. - Documentation that member will have f/u visit every 4 months to assess adherence and response to therapy. - Approval durations shortened to 16 weeks. - Added note that if the Group does not have obesity coverage, copayment will be 50% of the Rx cost.	07.10.24	08.24

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.