

## Zepbound™ (tirzepatide) for weight loss – New drug approval

- On November 8, 2023, the [FDA announced](#) the approval of [Eli Lilly's Zepbound \(tirzepatide\)](#), 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<sup>2</sup> or greater (obesity)
  - 27 kg/m<sup>2</sup> or greater (overweight) in the presence of at least one weight-related comorbid condition (eg, hypertension, dyslipidemia, type 2 diabetes mellitus (T2DM), obstructive sleep apnea, or cardiovascular disease).
- Zepbound contains tirzepatide, which is also approved under the brand name [Mounjaro™](#), for treatment of T2DM. Coadministration of Zepbound with other tirzepatide-containing products or with any glucagonlike peptide-1 (GLP-1) receptor agonist is not recommended.
- The safety and efficacy of Zepbound in combination with other products intended for weight management, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established.
- Zepbound has not been studied in patients with a history of pancreatitis.
- The efficacy of Zepbound was established in two randomized, double-blind, placebo-controlled trials (Study 1 and Study 2), in which weight reduction was assessed after 72 weeks of treatment (at least 52 weeks at maintenance dose). In both studies, the primary endpoint was the mean percent change in body weight and the percentage of patients achieving ≥ 5% weight reduction from baseline to week 72.
- Study 1 included 2,539 adult patients with obesity (BMI ≥ 30 kg/m<sup>2</sup>), or with overweight (BMI 27 to < 30 kg/m<sup>2</sup>) and at least one weight-related comorbid condition, such as dyslipidemia, hypertension, obstructive sleep apnea, or cardiovascular disease; patients with T2DM were excluded. Patients were randomized to Zepbound 5 mg, Zepbound 10 mg, Zepbound 15 mg, or placebo once weekly.

Body weight	Placebo	Zepbound 5 mg	Zepbound 10 mg	Zepbound 15 mg
Body weight				
Baseline mean (kg)	104.8	102.9	105.8	105.6
% Change from baseline	-3.1	-15.0	-19.5	-20.9
% Difference from placebo (95% CI)	--	-11.9 (-13.4, -10.4)*	-16.4 (-17.9, -14.8)*	-17.8 (-19.3, -16.3)*
% of patients losing ≥ 5% body weight	34.5	85.1	88.9	90.9
% Difference from placebo (95% CI)	--	50.3 (44.3, 56.2)*	54.6 (49.1, 60.0)*	56.4 (50.9, 62.0)*

\* p-value < 0.001

- Study 2 included 938 adult patients with BMI ≥ 27 kg/m<sup>2</sup> and T2DM. Patients were randomized to Zepbound 10 mg, Zepbound 15 mg, or placebo once weekly.

Body weight	Placebo	Zepbound 10 mg	Zepbound 15 mg
Body weight			
Baseline mean (kg)	101.7	100.9	99.6
% Change from baseline	-3.2	-12.8	-14.7
% Difference from placebo (95% CI)	--	-9.6 (-11.1, -8.1)*	-11.6 (-13.0, -10.1)*
% of patients losing ≥ 5% body weight	32.5	79.2	82.8
% Difference from placebo (95% CI)	--	46.8 (39.5, 54.1)*	50.4 (43.1, 57.8)*

\* p-value < 0.001

- Zepbound carries a boxed warning for risk of thyroid C-cell tumors.
- Zepbound is contraindicated in patients with:
  - A 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.
- Additional warnings and precautions for Zepbound include severe gastrointestinal disease; acute kidney injury; acute gallbladder disease; acute pancreatitis; hypersensitivity reactions; hypoglycemia; diabetic retinopathy complications in patients with T2DM; and suicidal behavior and ideation.
- The most common adverse reactions (≥ 5%) with Zepbound use were nausea, diarrhea, vomiting, constipation, abdominal pain, dyspepsia, injection site reactions, fatigue, hypersensitivity reactions, eructation, hair loss, and gastroesophageal reflux disease.
- The recommended starting dosage of Zepbound is 2.5 mg injected subcutaneously (SC) once weekly. The 2.5 mg dosage is for treatment initiation and is not intended for chronic weight management. After 4 weeks, the dosage should be increased to 5 mg injected 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 of Zepbound in adults are 5 mg, 10 mg, or 15 mg once weekly.
  - Treatment response and tolerability should be considered when selecting the maintenance dosage. If patients do not tolerate a maintenance dosage, a lower maintenance dosage should be considered.
  - The maximum dosage of Zepbound is 15 mg once weekly.
- Eli Lilly has announced that the list price of Zepbound will be \$1,059.87 per package (containing 4 weekly pens).
- Eli Lilly plans to launch Zepbound by end of year. Zepbound will be available as 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, and 15 mg (per 0.5 mL) single-dose pens.



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