once weekly

Pr zepbound®

(tirzepatide) injection

ZEPBOUND AT A GLANCE

Zepbound (tirzepatide injection) is indicated for once-weekly administration for chronic weight management, including weight loss and weight maintenance, as an adjunct to a reduced-calorie diet and increased physical activity, in adults with an initial body mass index (BMI) of:[1]

- 30 kg/m^2 or greater (obesity) or
- 27 kg/m^2 to less than 30 kg/m^2 (overweight)

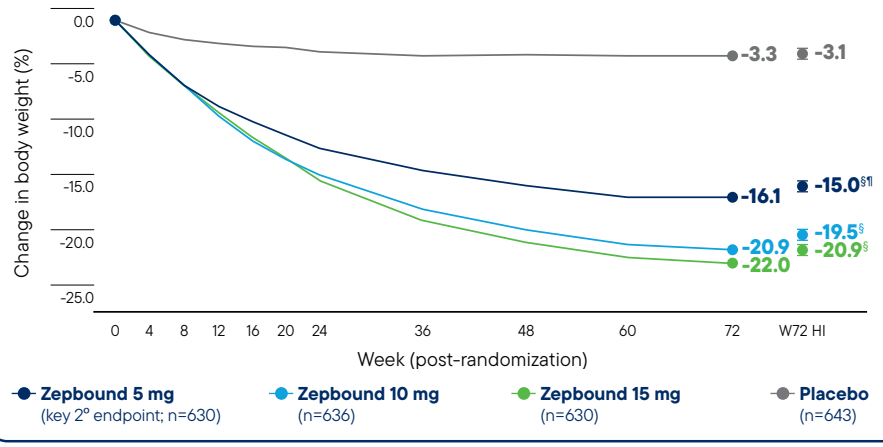
in the presence of at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, prediabetes, T2DM, obstructive sleep apnea, or cardiovascular disease)

Zepbound contains tirzepatide; coadministration with other tirzepatide-containing products (e.g., Mounjaro®) or with any GLP-1 receptor agonist is not recommended.

SURMOUNT-1 TRIAL: Zepbound vs. placebo*

Adults with obesity or with overweight and ≥1 weight-related comorbid condition[1]

Demonstrated change in body weight at Week 72 vs. placebo†‡



Adapted from the Zepbound Product Monograph.

† The intention-to-treat population includes all randomly assigned patients. For SURMOUNT-1 at Week 72, body weight was missing for 21.6%, 10.2%, 10.5%, and 9.4% of patients randomly assigned to placebo and to Zepbound 5 mg, 10 mg, and 15 mg, respectively. The missing values were imputed by a hybrid approach using retrieved dropouts from the same treatment group (if missing not due to COVID-19) or using all non-missing data assuming missing at random (for missing solely due to COVID-19).

‡ Least squares mean from ANCOVA adjusted for baseline value and other stratification factors.

§ $p<0.001$ (unadjusted 2-sided) for superiority, controlled for type I error rate.

¶ Data provided for 5 mg was a key 2° endpoint, controlled for type I error rate.

Note: (1) Observed mean value from Week 0 to 72; (2) LSM ± SE at Week 72 HI.

15–21% body weight reduction
was seen with Zepbound vs. 3.1% with placebo

SURMOUNT-5 TRIAL: Zepbound MTD vs. Wegovy® MTD||

Head-to-head, open-label trial in adults with obesity or with overweight and ≥1 weight-related comorbid condition (excluding T2DM)[2]

Zepbound MTD (maximum tolerated dose, 10 mg or 15 mg) vs. Wegovy MTD (1.7 mg or 2.4 mg)[2]

Demonstrated change in body weight at Week 72#

Zepbound MTD (10 mg or 15 mg; n=374)	Wegovy MTD (1.7 mg or 2.4 mg; n=376)
-20.2%	**-13.7%**

-6.5% treatment difference (95% CI: -8.1, -4.9); $p<0.001$**

LSM percent change from baseline; derived with an analysis-of-covariance model for modified treatment-regimen estimand.

** Estimated treatment difference between groups; $p<0.001$ vs. Wegovy.

Zepbound MTD demonstrated superior body weight reduction vs. Wegovy MTD

Patients can start Zepbound for as low as $300/month with the Savings Card†††‡‡‡

See SURMOUNT-1 and SURMOUNT-5 study designs on reverse.

ANCOVA=analysis of covariance; CI=confidence interval; GLP-1=glucagon-like peptide-1; HI=hybrid imputation; LSM=least squares mean; SE=standard error; T2DM=type 2 diabetes mellitus; W72=Week 72.

†† Exclusions and exceptions may apply. Estimated price based on retail pharmacy averages for 28-day supply. Prices vary by pharmacy and insurance coverage. Dispensing fees not included.

EXPLORE DOSING AND MORE AT **ZEPBOUND.CA**‡‡

FIRST & ONLY

The first and only single-molecule GIP/GLP-1 receptor agonist in chronic weight management[1,3]

Clinical use:

Limitations of use: 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.

The safety and efficacy of Zepbound have not been studied in pediatric patients. Zepbound is not indicated for use in pediatric patients.

No overall differences in safety or efficacy have been observed in clinical trial patients ≥65 years of age compared to younger patients.

Contraindications:

- Personal or family history of medullary thyroid carcinoma (MTC) or multiple endocrine neoplasia syndrome type 2 (MEN 2)
- Pregnancy or breastfeeding
- Hypersensitivity to tirzepatide, any ingredient in the formulation, including any nonmedicinal ingredient (e.g., benzyl alcohol), or component of the container

Most serious warnings and precautions:

Risk of thyroid C-cell tumours: Tirzepatide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumours (adenomas and carcinomas) at clinically relevant exposures in male and female rats. It is unknown whether Zepbound causes thyroid C-cell tumours, including MTC in humans; human relevance of tirzepatide-induced rodent thyroid C-cell tumours has not been determined. It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate human risk of thyroid C-cell tumours. Patients should be counselled regarding the risk and symptoms of thyroid tumours.

Other relevant warnings and precautions:

- Zepbound KwikPen® contains benzyl alcohol, which may cause allergic reactions; risk of metabolic acidosis in patients with hepatic or renal impairment
- Should not be administered intramuscularly or intravenously
- Increased heart rate
- Driving and operating machinery
- Hypoglycemia with concomitant use of insulin secretagogues or insulin in patients with T2DM
- Use with other incretin drugs
- GI and malnutrition events, including severe events
- Cholelithiasis or cholecystitis
- Acute pancreatitis
- Hypersensitivity reactions: anaphylaxis/angioedema
- Diabetic retinopathy complications in patients with T2DM; use with caution
- Aspiration during general anesthesia or deep sedation
- Suicidal ideation and behaviour; monitor patients and discontinue in those who experience suicidal thoughts/behaviours
- Acute kidney injury; monitor renal function in patients reporting ARs that could lead to volume depletion
- Women of childbearing potential
- Hepatic impairment

For more information:

Please consult the Product Monograph at http://pi.lilly.com/ca/zepbound-ca-pm.pdf for important information relating to adverse events, drug interactions, and dosing, which have not been discussed in this piece. The Product Monograph is also available by calling 1-888-545-5972.

AR=adverse reaction; GI=gastrointestinal; GIP=glucose-dependent insulinotropic polypeptide; QW=once weekly; Q4W=every 4 weeks.

* SURMOUNT-1: randomized, double-blind, placebo-controlled, 72-week trial in 2,539 adult patients with obesity (BMI ≥30 kg/m^2), or with overweight (BMI 27 to <30 kg/m^2) and ≥1 weight-related comorbid condition (e.g., dyslipidemia, hypertension, obstructive sleep apnea, cardiovascular disease); patients with T2DM were excluded. Patients were randomized 1:1:1:1 to once-weekly Zepbound 5 mg, 10 mg, or 15 mg, or placebo with an escalation period of up to 20 weeks followed by the maintenance period. All patients received a standard lifestyle intervention (i.e., instruction on a reduced-calorie diet [~500 kcal/day deficit]; increased physical activity counselling [≥150 min/week recommended]), along with counselling on behaviour modification strategies, that began with the first dose of study medication or placebo and continued throughout the trial. Weight reduction was assessed after 72 weeks of treatment (≥52 weeks at maintenance dose). Co-primary efficacy endpoints at Week 72 were mean percent change in body weight and percentage of patients achieving ≥5% weight reduction from baseline with Zepbound 10 mg and/or 15 mg.

|| SURMOUNT-5: phase 3b, open-label, multicentre, randomized, comparator-controlled, 72-week trial in 751 adults with obesity (BMI ≥30 kg/m^2) or with overweight (BMI 27 to <30 kg/m^2) and ≥1 weight-related complication (dyslipidemia, hypertension, obstructive sleep apnea, cardiovascular disease), and reported ≥1 unsuccessful dietary effort for weight reduction. Patients with T2DM were excluded. Patients were randomized 1:1 to subcutaneous administration of MTD of Zepbound (10 mg or 15 mg) QW or of Wegovy (1.7 mg or 2.4 mg) QW. Zepbound was initiated at the 2.5 mg QW dosage and increased in 2.5 mg increments Q4W until MTD of 10 mg or 15 mg was reached. Wegovy was initiated at the 0.25 mg QW dosage and increased Q4W in accordance with the recommended dosing regimen until the 2.4 mg dosage was reached. If unacceptable side effects were associated with the 2.4 mg dosage, the subject could receive 1.7 mg as the maintenance dosage, an approach consistent with the STEP 1 trial. Primary endpoint was percent change from baseline at Week 72 (Zepbound vs. Wegovy).

‡‡ The landing page of zepbound.ca is open to the general public.

References: 1. Current Zepbound® Product Monograph. Eli Lilly Canada Inc. **2.** Aronne LJ, et al. Tirzepatide as compared with semaglutide for the treatment of obesity. *N Engl J Med* 2025;393:26–36. **3.** Data on file (First and only). Eli Lilly Canada Inc. February 3, 2025.

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REVIEWED BY PAAB

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