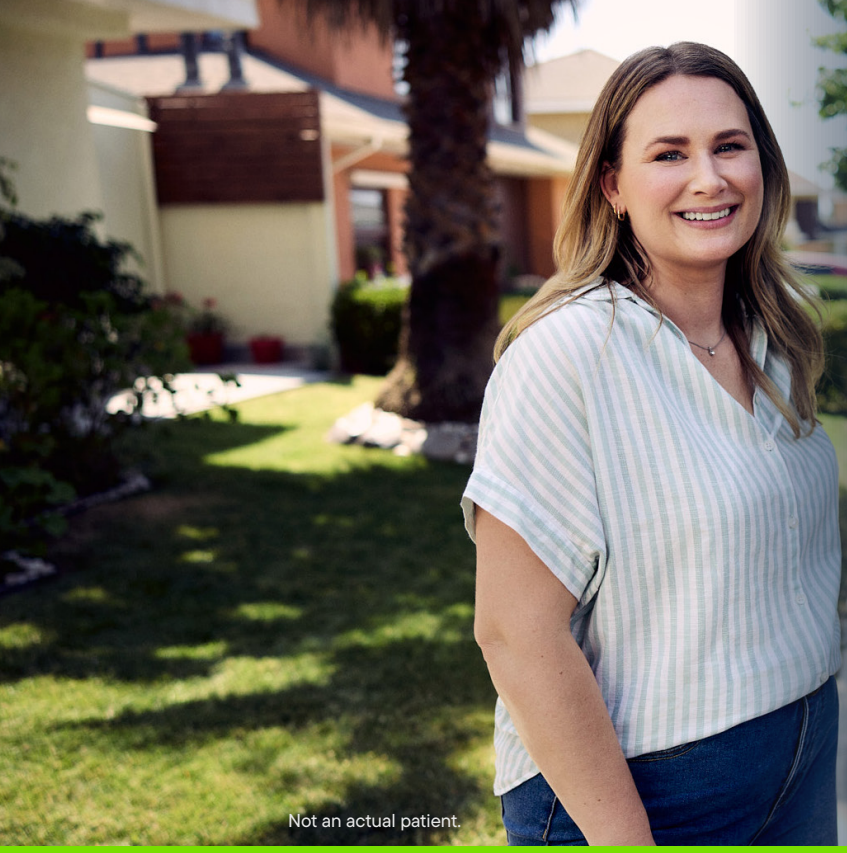


# Prior Authorization Resource Guide

*Help your patients get started on* ***Zepbound®*** *(tirzepatide) injection*

## Indication

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.

## Limitations of Use

Zepbound contains tirzepatide. Coadministration with other tirzepatide-containing products or with any glucagon-like peptide-1 (GLP-1) receptor agonist is not recommended.

## Select Important Safety Information

**WARNING: 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.**

**Please see Important Safety Information throughout, including Boxed Warning about possible thyroid tumors, including thyroid cancer. Please see accompanying Prescribing Information, including Boxed Warning, and Medication Guide.**

**Please see Instructions for Use.**

Lilly
A MEDICINE COMPANY

once weekly
zepbound®
(tirzepatide) injection 0.5 mL
2.5 mg | 5 mg | 7.5 mg | 10 mg | 12.5 mg | 15 mg

A Lilly Medicine

# Product Information[1]

## MEDICATION NAME

Zepbound® (tirzepatide)

## Indication

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.

## Limitations of Use

Zepbound contains tirzepatide. Coadministration with other tirzepatide-containing products or with any glucagon-like peptide-1 (GLP-1) receptor agonist is not recommended.

## STRENGTHS

| Available dosing strengths | NDC |
|---|---|
| 2.5 mg/0.5 mL in a single-dose pen | 0002-2506-80 |
| 5 mg/0.5 mL in a single-dose pen | 0002-2495-80 |
| 7.5 mg/0.5 mL in a single-dose pen | 0002-2484-80 |
| 10 mg/0.5 mL in a single-dose pen | 0002-2471-80 |
| 12.5 mg/0.5 mL in a single-dose pen | 0002-2460-80 |
| 15 mg/0.5 mL in a single-dose pen | 0002-2457-80 |

## Recommended maintenance dosages are 5 mg, 10 mg, or 15 mg:

- Initiate with the 2.5 mg dose
- After 4 weeks, increase to the 5 mg dose
- You can continue to increase the dose by 2.5 mg increments after at least 4 weeks on the current dose. The maximum dose is 15 mg
- Consider treatment response and tolerability when selecting maintenance dosage. If not tolerated, consider a lower maintenance dosage

**As an adjunct to a reduced-calorie diet and increased physical activity**

For adult patients with obesity (BMI of ≥30 kg/m$^2$) or with overweight (BMI of ≥27 kg/m$^2$) with at least 1 weight-related comorbidity.

The 2.5 mg dosage is for treatment initiation and is not intended for chronic weight management.[1]

The Zepbound vial is available in the 2.5 mg and 5 mg doses. The Zepbound pen is available in the 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, and 15 mg doses.[1]

NDC=National Drug Code.

## Select Important Safety Information

**Contraindications: Zepbound is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2, and in patients with known serious hypersensitivity to tirzepatide or any of the excipients in Zepbound. Serious hypersensitivity reactions including anaphylaxis and angioedema have been reported with tirzepatide.**

**Please see Important Safety Information throughout, including Boxed Warning about possible thyroid tumors, including thyroid cancer. Please see accompanying Prescribing Information, including Boxed Warning, and Medication Guide.**

**Please see Instructions for Use.**

once weekly zepbound® (tirzepatide) injection 0.5 mL

2.5 mg | 5 mg | 7.5 mg | 10 mg | 12.5 mg | 15 mg

A Lilly Medicine

# Submit Prior Authorization (PA)

This Zepbound PA checklist is intended to highlight important categorical information often considered in patient coverage decisions. Actual coverage requirements will vary.

## IMPORTANT INFORMATION THAT MAY BE REQUIRED FOR PA

| Zepbound PA checklist | Additional considerations |
|---|---|
| **Diagnosis** | • Documentation of an appropriate diagnosis and any weight-related comorbidities **(see *ICD-10* codes on pages 7-9 for commonly used codes)**<br>• Placing comorbidities in the primary diagnosis field may lead to PA denials |
| **Patient Weight & BMI** | • Patient weight and BMI supplement the diagnosis field in identifying eligible patients<br>• Different insurance plans may have different patient BMI requirements that result in coverage<br>• Baseline weight and BMI can be important information to document for both initial and reauthorization PAs |
| **Trial and/or Failure of Other Therapies** | • Other anti-obesity or weight loss medications the patient may have used in the past<br>• Examples include Alli® (orlistat), Contrave® (naltrexone HCl/bupropion HCl), Qsymia® (phentermine/topiramate extended-release capsules), Saxenda® (liraglutide), Xenical® (orlistat), Wegovy® (semaglutide), or Adipex-P®/Lomaira™ (phentermine HCl)[1] |
| **Lifestyle Modification** | • Any weight loss attempts by the patient in the past 3, 6, or 12 months<br>• Document whether you have instructed the patient to make concurrent lifestyle modifications such as a reduced-calorie diet and increased physical exercise while on Zepbound<br>• Implementation of diet (often defined as a 500 kcal deficit per day) and exercise (often defined as 150 minutes of activity per week) or enrollment in specific payer, employer, or patient-initiated programs should also be documented |

[1] Other product names mentioned herein are the trademarks of their respective owners.

### Select Important Safety Information

**Risk of Thyroid C-cell Tumors:** 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. Such monitoring may increase the risk of unnecessary procedures, due to the low test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin values may indicate MTC and patients with MTC usually have calcitonin values >50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

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**Please see Instructions for Use.**

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# Submit PA (continued)

| Zepbound PA checklist | Additional considerations |
|---|---|
| **Continuation of Therapy** | • Continuation of therapy designations are often available for patients who are already taking Zebound<br>• For reauthorizations, document the percentage of weight loss from baseline weight and for how long a patient has maintained on a stable maintenance dose (5 mg, 10 mg, or 15 mg) |
| **Drug Combinations** | Whether Zepbound is being co-administered with other drugs. Note:<br>• Coadministration with other tirzepatide-containing products or any GLP-1 receptor agonist is not recommended[1]<br>• The safety and efficacy of coadministration with other products for weight management have not been established[1] |

## KEY REMINDERS

- You will likely need to complete a PA request before your patient's insurance will cover Zepbound
- It is important to accurately provide detailed information in the PA request to help your patients access Zepbound
- Double check if payers require clinical documentation of certain information
- Incomplete or incorrect documentation may result in a denied claim

### EXPLORE FORMULARY COVERAGE & ZEPBOUND RESOURCES

Visit zepbound.lilly.com/hcp/coverage-savings

- Look Up **formulary coverage** in your area
- **See additional Zepbound resources:** Prior Authorization Guide, Letter of Medical Necessity Guide, and more

### HAVE ADDITIONAL QUESTIONS? LIVE PHONE AGENTS CAN HELP

**Call 1-800-LillyRx** to speak with a live agent for benefits verification, PA support, and more. To reach a Lilly Support Services agent, choose the options for HCP, Zepbound, and then Access and Affordability.

### Select Important Safety Information

**Severe Gastrointestinal Adverse Reactions:** Use of Zepbound has been associated with gastrointestinal adverse reactions, sometimes severe. In a pool of two Zepbound clinical trials (Study 1 and Study 2), severe gastrointestinal adverse reactions were reported more frequently among patients receiving Zepbound (5 mg 1.7%, 10 mg 2.5%, 15 mg 3.1%) than placebo (1.0%). Zepbound has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis, and is therefore not recommended in these patients.

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# Submit PA (continued)

## COMMONLY SEEN ZEPBOUND PA CRITERIA ACROSS MAJOR NATIONAL PAYER FORMULARIES

### BMI Cutoffs

- Aligned with Zepbound-labeled indication—obesity (BMI ≥30 kg/m$^2$) or overweight (≥27 kg/m$^2$) with at least 1 weight-related comorbidity)[1]
- Documentation of BMI is required
- Documentation of any weight-related comorbidities is required (the list of qualifying comorbidities will vary between formularies)

### Behavioral Modification Requirements

- Patient has participated in weight management program or diet/exercise for at least 3-6 months prior to therapy
- Medication will be used alongside diet and exercise

### Reauthorization

- Documentation that patient has lost or maintained a loss of at least 5% from their baseline weight
- Initial authorization duration: ~6-8 months
- Some reauthorizations may be dependent on patients being stable on a maintenance dose (5 mg, 10 mg, or 15 mg) for several months

### Other

- Age: 18+
- No concurrent use of other GLP-1 agonists or other weight loss medication
- No history of pancreatitis
- Step edits not usually required
- No/few specialist prescribing restrictions

## Select Important Safety Information

**Acute Kidney Injury:** Use of Zepbound has been associated with acute kidney injury, which can result from dehydration due to gastrointestinal adverse reactions to Zepbound, including nausea, vomiting, and diarrhea. In patients treated with GLP-1 receptor agonists, there have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which may sometimes require hemodialysis. Some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Monitor renal function in patients reporting adverse reactions to Zepbound that could lead to volume depletion.

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# Submit PA (continued)

## EMPOWER YOUR PATIENTS WITH INFORMATION IF YOU USE COVERMYMEDS FOR PAs

Many patients appreciate insights into their healthcare journey, including the status of their prior authorizations. CoverMyMeds now offers providers the ability to notify patients of their PA outcome in real time via text or email.

## No more back-and-forth phone calls. Here's how it works:

1. Start a PA request at **covermymeds.com** or open a pharmacy-initiated request.
2. With patient consent, **select option** on PA page **to inform patient** of PA outcome.
3. Enter the **patient contact** information.
4. **Submit the PA** to the plan; once plan determination is received, the patient and provider's office are notified.

**HAVE QUESTIONS FOR COVERMYMEDS?**

Live Chat: **covermymeds.com** | Phone **1-866-452-5017**
8 AM to 11 PM EST Monday-Friday and 8 AM to 6 PM EST Saturday

### Select Important Safety Information

**Acute Gallbladder Disease:** Treatment with Zepbound and GLP-1 receptor agonists is associated with an increased occurrence of acute gallbladder disease. In a pool of two clinical trials of Zepbound (Study 1 and Study 2), cholelithiasis was reported in 1.1% of Zepbound-treated patients and 1.0% of placebo-treated patients, cholecystitis was reported in 0.7% of Zepbound-treated patients and 0.2% of placebo-treated patients, and cholecystectomy was reported in 0.2% of Zepbound-treated patients and no placebo-treated patients. Acute gallbladder events were associated with weight reduction. If cholecystitis is suspected, gallbladder diagnostic studies and appropriate clinical follow-up are indicated.

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A Lilly Medicine

# Submit PA (continued)

## *ICD-10* CODES[2]

Below are commonly identified *ICD-10* codes related to Zepbound. Some less commonly used codes may be missing. For additional codes, please refer to a coding resource.*

| Code | Code description |
|---|---|
| E66.0<br>- E66.01<br>- E66.09 | Obesity due to excess calories<br>– Morbid (severe) obesity due to excess calories<br>– Other obesity due to excess calories |
| E66.1 | Drug-induced obesity |
| E66.2 | Morbid (severe) obesity with alveolar hypoventilation |
| E66.3 | Overweight |
| E66.8<br>- E66.81<br>- E66.811<br>- E66.812<br>- E66.813<br>- E66.89 | Other obesity (These codes should be available for use starting 10/1/24)<br>(Obesity class)<br>(Obesity, class 1)<br>(Obesity, class 2)<br>(Obesity, class 3)<br>(Other obesity not elsewhere classified) |
| E66.9 | Obesity, unspecified (can be used once for initial visit only) |

*The *ICD-10-CM* code list is not all-inclusive. Appropriate codes vary by patient, payer, and setting for care. Correct coding is the responsibility of the provider submitting the claim. Eli Lilly and Company does not make any representation or guarantee for reimbursement or coverage.

*ICD-10-CM=International Classification of Diseases, Tenth Revision, Clinical Modification.*

## Indication

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.

## Limitations of Use

Zepbound contains tirzepatide. Coadministration with other tirzepatide-containing products or with any glucagon-like peptide-1 (GLP-1) receptor agonist is not recommended.

## Select Important Safety Information

**Acute Pancreatitis:** Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists or tirzepatide. In clinical trials of tirzepatide for a different indication, 14 events of acute pancreatitis were confirmed by adjudication in 13 tirzepatide-treated patients (0.23 patients per 100 years of exposure) versus 3 events in 3 comparator-treated patients (0.11 patients per 100 years of exposure). In a pool of two Zepbound clinical trials (Study 1 and Study 2), 0.2% of Zepbound-treated patients had acute pancreatitis confirmed by adjudication (0.14 patients per 100 years of exposure) versus 0.2% of placebo-treated patients (0.15 patients per 100 years of exposure). Zepbound has not been studied in patients with a prior history of pancreatitis. It is unknown if patients with a history of pancreatitis are at higher risk for development of pancreatitis on Zepbound. Observe patients for signs and symptoms of pancreatitis, including persistent severe abdominal pain sometimes radiating to the back, which may or may not be accompanied by vomiting. If pancreatitis is suspected, discontinue Zepbound and initiate appropriate management. If the diagnosis of pancreatitis is confirmed, Zepbound should not be restarted.

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# Submit PA (continued)

## *ICD-10* CODES[2]

Below are commonly identified *ICD-10* codes related to Zepbound. Some less commonly used codes may be missing. For additional codes, please refer to a coding resource.*

### BMI REPORTING FOR ADULT BMI ≥27 kg/m²

| Code | Code description | Code | Code description |
|---|---|---|---|
| Z68.27 | BMI 27.0-27.9 | Z68.36 | BMI 36.0-36.9 |
| Z68.28 | BMI 28.0-28.9 | Z68.37 | BMI 37.0-37.9 |
| Z68.29 | BMI 29.0-29.9 | Z68.38 | BMI 38.0-38.9 |
| Z68.30 | BMI 30.0-30.9 | Z68.39 | BMI 39.0-39.9 |
| Z68.31 | BMI 31.0-31.9 | Z68.41 | BMI 40.0-44.9 |
| Z68.32 | BMI 32.0-32.9 | Z68.42 | BMI 45.0-49.9 |
| Z68.33 | BMI 33.0-33.9 | Z68.43 | BMI 50.0-59.9 |
| Z68.34 | BMI 34.0-34.9 | Z68.44 | BMI 60.0-69.9 |
| Z68.35 | BMI 35.0-35.9 | Z68.45 | BMI ≥70 |

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### Indication

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### Limitations of Use

Zepbound contains tirzepatide. Coadministration with other tirzepatide-containing products or with any glucagon-like peptide-1 (GLP-1) receptor agonist is not recommended.

### Select Important Safety Information

**Hypersensitivity Reactions:** There have been postmarketing reports of serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) in patients treated with tirzepatide. In a pool of two Zepbound clinical trials (Study 1 and Study 2), 0.1% of Zepbound-treated patients had severe hypersensitivity reactions compared to no placebo-treated patients. If hypersensitivity reactions occur, advise patients to promptly seek medical attention and discontinue use of Zepbound. Do not use in patients with a previous serious hypersensitivity reaction to tirzepatide or any of the excipients in Zepbound. Use caution in patients with a history of angioedema or anaphylaxis with a GLP-1 receptor agonist because it is unknown if such patients will be predisposed to these reactions with Zepbound.

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# Submit PA (continued)

## *ICD-10* CODES[2]

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### CODES FOR SELECT WEIGHT-RELATED COMORBIDITIES

Zepbound is not indicated for treatment of these conditions.

| Code | Code description |
|---|---|
| I10 | Essential (primary) hypertension |
| E78.5 | Hyperlipidemia, unspecified |
| E11 | Type 2 diabetes mellitus |
| G47.33 | Obstructive sleep apnea (adult) (pediatric) |
| I51.9 | Heart disease, unspecified |

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### Limitations of Use

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### Select Important Safety Information

**Hypoglycemia:** Zepbound lowers blood glucose and can cause hypoglycemia. In a trial of patients with type 2 diabetes mellitus and BMI ≥27 kg/m$^2$ (Study 2), hypoglycemia (plasma glucose <54 mg/dL) was reported in 4.2% of Zepbound-treated patients versus 1.3% of placebo-treated patients. In this trial, patients taking Zepbound in combination with an insulin secretagogue (e.g., sulfonylurea) had increased risk of hypoglycemia (10.3%) compared to Zepbound-treated patients not taking a sulfonylurea (2.1%). There is also increased risk of hypoglycemia in patients treated with tirzepatide in combination with insulin. Hypoglycemia has also been associated with Zepbound and GLP-1 receptor agonists in adults without type 2 diabetes mellitus. Inform patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia. In patients with diabetes mellitus, monitor blood glucose prior to starting Zepbound and during Zepbound treatment. The risk of hypoglycemia may be lowered by a reduction in the dose of insulin or sulfonylurea (or other concomitantly administered insulin secretagogue).

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A Lilly Medicine

## Important Safety Information for Zepbound® (tirzepatide) injection

**WARNING: 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.**

**Contraindications: Zepbound is contraindicated in patients with a personal or family history of MTC or in patients with MEN 2, and in patients with known serious hypersensitivity to tirzepatide or any of the excipients in Zepbound. Serious hypersensitivity reactions including anaphylaxis and angioedema have been reported with tirzepatide.**

**Risk of Thyroid C-cell Tumors:** 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. Such monitoring may increase the risk of unnecessary procedures, due to the low test specificity for serum calcitonin and a high background incidence of thyroid disease. Significantly elevated serum calcitonin values may indicate MTC and patients with MTC usually have calcitonin values >50 ng/L. If serum calcitonin is measured and found to be elevated, the patient should be further evaluated. Patients with thyroid nodules noted on physical examination or neck imaging should also be further evaluated.

**Severe Gastrointestinal Adverse Reactions:** Use of Zepbound has been associated with gastrointestinal adverse reactions, sometimes severe. In a pool of two Zepbound clinical trials (Study 1 and Study 2), severe gastrointestinal adverse reactions were reported more frequently among patients receiving Zepbound (5 mg 1.7%, 10 mg 2.5%, 15 mg 3.1%) than placebo (1.0%). Zepbound has not been studied in patients with severe gastrointestinal disease, including severe gastroparesis, and is therefore not recommended in these patients.

**Acute Kidney Injury:** Use of Zepbound has been associated with acute kidney injury, which can result from dehydration due to gastrointestinal adverse reactions to Zepbound, including nausea, vomiting, and diarrhea. In patients treated with GLP-1 receptor agonists, there have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which may sometimes require hemodialysis. Some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Monitor renal function in patients reporting adverse reactions to Zepbound that could lead to volume depletion.

**Acute Gallbladder Disease:** Treatment with Zepbound and GLP-1 receptor agonists is associated with an increased occurrence of acute gallbladder disease. In a pool of two clinical trials of Zepbound (Study 1 and Study 2), cholelithiasis was reported in 1.1% of Zepbound-treated patients and 1.0% of placebo-treated patients, cholecystitis was reported in 0.7% of Zepbound-treated patients and 0.2% of placebo-treated patients, and cholecystectomy was reported in 0.2% of Zepbound-treated patients and no placebo-treated patients. Acute gallbladder events were associated with weight reduction. If cholecystitis is suspected, gallbladder diagnostic studies and appropriate clinical follow-up are indicated.

**Acute Pancreatitis:** Acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with GLP-1 receptor agonists or tirzepatide. In clinical trials of tirzepatide for a different indication, 14 events of acute pancreatitis were confirmed by adjudication in 13 tirzepatide-treated patients (0.23 patients per 100 years of exposure) versus 3 events in 3 comparator-treated patients (0.11 patients per 100 years of exposure). In a pool of two Zepbound clinical trials (Study 1 and Study 2), 0.2% of Zepbound-treated patients had acute pancreatitis confirmed by adjudication (0.14 patients per 100 years of exposure) versus 0.2% of placebo-treated patients (0.15 patients per 100 years of exposure). Zepbound has not been studied in patients with a prior history of pancreatitis. It is unknown if patients with a history of pancreatitis are at higher risk for development of pancreatitis on Zepbound. Observe patients for signs and symptoms of pancreatitis, including persistent severe abdominal pain sometimes radiating to the back, which may or may not be accompanied by vomiting. If pancreatitis is suspected, discontinue Zepbound and initiate appropriate management. If the diagnosis of pancreatitis is confirmed, Zepbound should not be restarted.

**Hypersensitivity Reactions:** There have been postmarketing reports of serious hypersensitivity reactions (e.g., anaphylaxis, angioedema) in patients treated with tirzepatide. In a pool of two Zepbound clinical trials (Study 1 and Study 2), 0.1% of Zepbound-treated patients had severe hypersensitivity reactions compared to no placebo-treated patients. If hypersensitivity

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**Please see Instructions for Use.**

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A Lilly Medicine

## Important Safety Information for Zepbound® (tirzepatide) injection (continued)

reactions occur, advise patients to promptly seek medical attention and discontinue use of Zepbound. Do not use in patients with a previous serious hypersensitivity reaction to tirzepatide or any of the excipients in Zepbound. Use caution in patients with a history of angioedema or anaphylaxis with a GLP-1 receptor agonist because it is unknown if such patients will be predisposed to these reactions with Zepbound.

**Hypoglycemia:** Zepbound lowers blood glucose and can cause hypoglycemia. In a trial of patients with type 2 diabetes mellitus and BMI ≥27 kg/m$^2$ (Study 2), hypoglycemia (plasma glucose <54 mg/dL) was reported in 4.2% of Zepbound-treated patients versus 1.3% of placebo-treated patients. In this trial, patients taking Zepbound in combination with an insulin secretagogue (e.g., sulfonylurea) had increased risk of hypoglycemia (10.3%) compared to Zepbound-treated patients not taking a sulfonylurea (2.1%). There is also increased risk of hypoglycemia in patients treated with tirzepatide in combination with insulin. Hypoglycemia has also been associated with Zepbound and GLP-1 receptor agonists in adults without type 2 diabetes mellitus. Inform patients of the risk of hypoglycemia and educate them on the signs and symptoms of hypoglycemia. In patients with diabetes mellitus, monitor blood glucose prior to starting Zepbound and during Zepbound treatment. The risk of hypoglycemia may be lowered by a reduction in the dose of insulin or sulfonylurea (or other concomitantly administered insulin secretagogue).

**Diabetic Retinopathy Complications in Patients with Type 2 Diabetes Mellitus:** Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy. Tirzepatide has not been studied in patients with non-proliferative diabetic retinopathy requiring acute therapy, proliferative diabetic retinopathy, or diabetic macular edema. Patients with a history of diabetic retinopathy should be monitored for progression of diabetic retinopathy.

**Suicidal Behavior and Ideation:** Suicidal behavior and ideation have been reported in clinical trials with other weight management products. Monitor patients treated with Zepbound for the emergence or worsening of depression, suicidal thoughts or behaviors, and/or any unusual changes in mood or behavior. Discontinue Zepbound in patients who experience suicidal thoughts or behaviors. Avoid Zepbound in patients with a history of suicidal attempts or active suicidal ideation.

**Pulmonary Aspiration During General Anesthesia or Deep Sedation:** Zepbound delays gastric emptying. There have been rare postmarketing reports of pulmonary aspiration in patients receiving GLP-1 receptor agonists undergoing elective surgeries or procedures requiring general anesthesia or deep sedation who had residual gastric contents despite reported adherence to preoperative fasting recommendations. Available data are insufficient to inform recommendations to mitigate the risk of pulmonary aspiration during general anesthesia or deep sedation in patients taking Zepbound, including whether modifying preoperative fasting recommendations or temporarily discontinuing Zepbound could reduce the incidence of retained gastric contents. Instruct patients to inform healthcare providers prior to any planned surgeries or procedures if they are taking Zepbound.

**Most common adverse reactions:** The most common adverse reactions, reported in ≥5% of patients treated with Zepbound are: nausea, diarrhea, vomiting, constipation, abdominal pain, dyspepsia, injection site reactions, fatigue, hypersensitivity reactions, eructation, hair loss, and gastroesophageal reflux disease.

**Drug Interactions:** Zepbound lowers blood glucose. When initiating Zepbound, consider reducing the dose of concomitantly administered insulin secretagogues (e.g., sulfonylureas) or insulin to reduce the risk of hypoglycemia. Zepbound delays gastric emptying and thereby has the potential to impact the absorption of concomitantly administered oral medications. Caution should be exercised when oral medications are concomitantly administered with Zepbound. Monitor patients on oral medications dependent on threshold concentrations for efficacy and those with a narrow therapeutic index (e.g., warfarin) when concomitantly administered with Zepbound.

**Pregnancy:** Advise pregnant patients that weight loss is not recommended during pregnancy and to discontinue Zepbound when a pregnancy is recognized. Available data with tirzepatide in pregnant patients are insufficient to evaluate for a drug-related risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Based on animal reproduction studies, there may be risks to the fetus from exposure to tirzepatide during pregnancy. There will be a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to Zepbound (tirzepatide) during pregnancy. Pregnant patients exposed to Zepbound and healthcare providers are encouraged to contact Eli Lilly and Company at 1-800-LillyRx (1-800-545-5979).

**Lactation:** There are no data on the presence of tirzepatide or its metabolites in animal or human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Zepbound and any potential adverse effects on the breastfed infant from Zepbound or from the underlying maternal condition.

**Females and Males of Reproductive Potential:** Use of Zepbound may reduce the efficacy of oral hormonal contraceptives due to delayed gastric emptying. This delay is largest after the first dose and diminishes over time. Advise patients using oral hormonal contraceptives to switch to a non-oral contraceptive method or add a barrier method of contraception, for 4 weeks after initiation with Zepbound and for 4 weeks after each dose escalation.

**Pediatric Use:** The safety and effectiveness of Zepbound have not been established in pediatric patients.

**Please see accompanying Prescribing Information, including Boxed Warning about possible thyroid tumors, including thyroid cancer, and Medication Guide.**

**Please see Instructions for Use.**

ZP HCP ISI 18OCT2024

once weekly
zepbound®
(tirzepatide) injection 0.5 mL
2.5 mg | 5 mg | 7.5 mg | 10 mg | 12.5 mg | 15 mg

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**References: 1.** Zepbound. Prescribing Information. Lilly USA, LLC. **2.** CDC. ICD-10 tabular list of diseases and injuries. Accessed May 10, 2024. https://ftp.cdc.gov/pub/health_statistics/nchs/publications/ICD10CM/2022/icd10cm-tabular-2022-April-1.pdf



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