FDA approves Zepbound® (tirzepatide) as the first and only prescription medicine for moderate-to-severe obstructive sleep apnea in adults with obesity

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Averaging up to 20% of weight loss, adults taking Zepbound had at least 25 fewer breathing interruptions each hour as they slept

Up to 50% of adults taking Zepbound no longer had symptoms associated with OSA after one year

INDIANAPOLIS, Dec. 20, 2024 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) today announced the U.S. Food and Drug Administration (FDA) approved Zepbound® (tirzepatide) as the first and only prescription medicine for adults with moderate-to-severe obstructive sleep apnea (OSA) and obesity.[1] Zepbound may help adults with moderate-to-severe obstructive sleep apnea and obesity improve their sleep disorder. It should be used with a reduced-calorie diet and increased physical activity.

"Too often, OSA is brushed off as 'just snoring' — but it's far more than that," said Julie Flygare, J.D., president and CEO of Project Sleep. "It's important to understand OSA symptoms and know that treatments are available, including new options like Zepbound. We hope this will spark more meaningful conversations between patients and health care providers and ultimately lead to better health outcomes."

OSA is a sleep-related breathing disorder characterized by complete or partial collapses of the upper airway during sleep, which can lead to pauses in breathing (apnea) or shallow breathing (hypopnea) and a potential decrease in oxygen saturation and/or waking from sleep. One of the hallmarks of OSA is snoring, but fatigue, excessive daytime sleepiness and disrupted sleep are also key symptoms, making this serious condition easily overlooked.

"Today, many cases of OSA go undiagnosed and untreated, leaving millions at risk for serious health consequences," said Patrik Jonsson, executive vice president, and president of Lilly Cardiometabolic Health and Lilly USA. "Zepbound is the first medication that significantly improves moderate-to-severe OSA and aids in long-term weight loss in adults with obesity. Nearly half of clinical trial patients saw such improvements that they no longer had symptoms associated with OSA, marking a critical step forward in reducing the burden of this disease and its interconnected health challenges."

This approval was based on results from the SURMOUNT-OSA phase 3 clinical trials, which evaluated Zepbound (10 mg or 15 mg) for the treatment of moderate-to-severe OSA in adults with obesity, with and without positive airway pressure (PAP) therapy over the course of a year. Zepbound was about five times more effective than placebo in reducing breathing disruptions in adults not on PAP therapy, leading to 25 fewer breathing disruptions per hour with Zepbound and five with placebo. In adults on PAP therapy, Zepbound led to 29 fewer breathing disruptions per hour compared to six with placebo. After one year, 42% of adults on Zepbound and 50% of adults on Zepbound with PAP therapy experienced remission or mild, non-symptomatic OSA, compared to 16% and 14% on placebo, respectively.

In addition to improved OSA symptoms, adults on Zepbound lost an average of 45 lbs (18%) of their body weight, while adults on Zepbound with PAP therapy lost an average of 50 lbs (20%) of their body weight, compared to 4 lbs (2%) and 6 lbs (2%) on placebo, respectively.

Zepbound contains tirzepatide and should not be used with other tirzepatide-containing products or any GLP-1 receptor agonist medicines. It is not known if it is safe and effective for use in children. Zepbound may cause tumors in the thyroid, including thyroid cancer. Watch for possible symptoms, such as a lump or swelling in the neck, hoarseness, trouble swallowing or shortness of breath. If you have any of these symptoms, tell your health care provider. Do not use Zepbound if you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC). Do not use Zepbound if you have Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Do not use Zepbound if you have had a serious allergic reaction to tirzepatide or any of the ingredients in Zepbound. Stomach problems, sometimes severe, have been reported in people who use Zepbound. Tell your health care provider if you have stomach problems that are severe or will not go away. The most common side effects of Zepbound include nausea, diarrhea, vomiting, constipation, stomach (abdominal) pain, indigestion, injection site reactions, feeling tired, allergic reactions, belching, hair loss and heartburn. These are not all the possible side effects of Zepbound. Talk to your health care provider about any side effect that bothers you or doesn't go away.

Please see indication and safety summary with warning below and full prescribing information and medication guide.

This is the second indication in the U.S. for Zepbound in just over a year, following the FDA approval for adults with obesity or overweight who also have weight-related medical problems in November 2023. To learn more about Zepbound and how it can treat moderate-to-severe OSA and obesity, please visit Zepbound.lilly.com.

About SURMOUNT-OSA
SURMOUNT-OSA (NCT05412004) was a multi-center, randomized, double-blind, parallel, placebo-master protocol comparing the efficacy and safety of Zepbound® (tirzepatide) to placebo in adults living with moderate-to-severe obstructive sleep apnea (OSA) and obesity who were unable or unwilling to use positive airway pressure (PAP) therapy (Study 1) and those who were and planned to stay on PAP therapy during the duration of the trial (Study 2). Under a master protocol, the trials randomized 469 participants across the U.S., Australia, Brazil, China, Czechia, Germany, Japan, Mexico and Taiwan in a 1:1 ratio to receive Zepbound maximum tolerated dose (MTD) of 10 mg or 15 mg or placebo. The primary objective of both studies was to demonstrate that Zepbound is superior in change in apnea-hypopnea index (AHI) from baseline at 52 weeks as compared to placebo.

SURMOUNT-OSA utilized an MTD of 10 mg or 15 mg once-weekly. The starting dose of 2.5 mg Zepbound was increased by 2.5 mg every four weeks until maximum tolerated dose was achieved. Participants who tolerated 15 mg continued on 15 mg as their MTD. Participants who tolerated 10 mg but

did not tolerate 15 mg continued on 10 mg as their MTD.

About Zepbound® (tirzepatide) injection
Zepbound® (tirzepatide) injection is FDA-approved to treat adults with moderate-to-severe obstructive sleep apnea and obesity. It is also approved 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.

Zepbound is the first and only dual-activating GIP (glucose-dependent insulinotropic polypeptide) and GLP-1 (glucagon-like peptide-1) obesity medication. Zepbound tackles an underlying cause of excess weight. It reduces appetite and how much you eat.

INDICATIONS AND SAFETY SUMMARY WITH WARNINGS
Zepbound® (ZEHP-bownd) is an injectable prescription medicine that may help adults with:

- obesity, or some adults with overweight who also have weight-related medical problems to lose excess body weight and keep the weight off.
- moderate-to-severe obstructive sleep apnea (OSA) and obesity to improve their OSA.

It should be used with a reduced-calorie diet and increased physical activity.

Zepbound contains tirzepatide and should not be used with other tirzepatide-containing products or any GLP-1 receptor agonist medicines. It is not known if Zepbound is safe and effective for use in children.

Warnings - Zepbound may cause tumors in the thyroid, including thyroid cancer. Watch for possible symptoms, such as a lump or swelling in the neck, hoarseness, trouble swallowing, or shortness of breath. If you have any of these symptoms, tell your healthcare provider.

- Do not use Zepbound if you or any of your family have ever had a type of thyroid cancer called medullary thyroid carcinoma (MTC).
- Do not use Zepbound if you have Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).
- Do not use Zepbound if you have had a serious allergic reaction to tirzepatide or any of the ingredients in Zepbound.

Zepbound may cause serious side effects, including:

Severe stomach problems. Stomach problems, sometimes severe, have been reported in people who use Zepbound. Tell your healthcare provider if you have stomach problems that are severe or will not go away.

Kidney problems (kidney failure). Diarrhea, nausea, and vomiting may cause a loss of fluids (dehydration), which may cause kidney problems. It is important for you to drink fluids to help reduce your chance of dehydration.

Gallbladder problems. Gallbladder problems have happened in some people who use Zepbound. Tell your healthcare provider right away if you get symptoms of gallbladder problems, which may include pain in your upper stomach (abdomen), fever, yellowing of skin or eyes (jaundice), or clay-colored stools.

Inflammation of the pancreas (pancreatitis). Stop using Zepbound and call your healthcare provider right away if you have severe pain in your stomach area (abdomen) that will not go away, with or without vomiting. You may feel the pain from your abdomen to your back.

Serious allergic reactions. Stop using Zepbound and get medical help right away if you have any symptoms of a serious allergic reaction, including swelling of your face, lips, tongue or throat, problems breathing or swallowing, severe rash or itching, fainting or feeling dizzy, or very rapid heartbeat.

Low blood sugar (hypoglycemia). Your risk for getting low blood sugar may be higher if you use Zepbound with medicines that can cause low blood sugar, such as a sulfonylurea or insulin. **Signs and symptoms of low blood sugar** may include dizziness or light-headedness, sweating, confusion or drowsiness, headache, blurred vision, slurred speech, shakiness, fast heartbeat, anxiety, irritability, mood changes, hunger, weakness or feeling jittery.

Changes in vision in patients with type 2 diabetes. Tell your healthcare provider if you have changes in vision during treatment with Zepbound.

Depression or thoughts of suicide. You should pay attention to changes in your mood, behaviors, feelings or thoughts. Call your healthcare provider right away if you have any mental changes that are new, worse, or worry you.

Food or liquid getting into the lungs during surgery or other procedures that use anesthesia or deep sleepiness (deep sedation). Zepbound may increase the chance of food getting into your lungs during surgery or other procedures. Tell all your healthcare providers that you are taking Zepbound before you are scheduled to have surgery or other procedures.

Common side effects
The most common side effects of Zepbound include nausea, diarrhea, vomiting, constipation, stomach (abdominal) pain, indigestion, injection site reactions, feeling tired, allergic reactions, belching, hair loss, and heartburn. These are not all the possible side effects of Zepbound. Talk to your healthcare provider about any side effect that bothers you or doesn't go away.

Tell your doctor if you have any side effects. **You can report side effects at 1-800-FDA-1088 or *www.fda.gov/medwatch*.**

Before using Zepbound

- **Your healthcare provider should show you how to use Zepbound before you use it for the first time.**
- **Tell your healthcare provider if you are taking medicines to treat diabetes including an insulin or sulfonylurea which could increase your risk of low blood sugar. Talk to your healthcare provider about low blood sugar levels**

and how to manage them.

- **If you take birth control pills by mouth, talk to your healthcare provider before you use Zepbound. Birth control pills may not work as well while using Zepbound.** Your healthcare provider may recommend another type of birth control for 4 weeks after you start Zepbound and for 4 weeks after each increase in your dose of Zepbound.

Review these questions with your healthcare provider:

❑ Do you have other medical conditions, including problems with your pancreas or kidneys, or severe problems with your stomach, such as slowed emptying of your stomach (gastroparesis) or problems digesting food?
❑ Do you take diabetes medicines, such as insulin or sulfonylureas?
❑ Do you have a history of diabetic retinopathy?
❑ Are you scheduled to have surgery or other procedures that use anesthesia or deep sleepiness (deep sedation)?
❑ Do you take any other prescription medicines or over-the-counter drugs, vitamins, or herbal supplements?
❑ Are you pregnant, plan to become pregnant, breastfeeding, or plan to breastfeed? Zepbound may harm your unborn baby. Tell your healthcare provider if you become pregnant while using Zepbound. It is not known if Zepbound passes into your breast milk. You should talk with your healthcare provider about the best way to feed your baby while using Zepbound.

- **Pregnancy Exposure Registry:** There will be a pregnancy exposure registry for women who have taken Zepbound during pregnancy. The purpose of this registry is to collect information about the health of you and your baby. Talk to your healthcare provider about how you can take part in this registry, or you may contact Lilly at 1-800-LillyRx (1-800-545-5979).

How to take

- Read the Instructions for Use that come with Zepbound.
- Use Zepbound exactly as your healthcare provider says.
- Use Zepbound with a reduced-calorie diet and increased physical activity.
- Zepbound is injected under the skin (subcutaneously) of your stomach (abdomen), thigh, or upper arm.
- **Use Zepbound 1 time each week, at any time of the day.**
- Change (rotate) your injection site with each weekly injection. **Do not** use the same site for each injection.
- If you take too much Zepbound, call your healthcare provider, seek medical advice promptly, or contact a Poison Center expert right away at 1-800-222-1222.

Zepbound injection is approved as a 2.5 mg, 5 mg, 7.5 mg, 10 mg, 12.5 mg, or 15 mg per 0.5 mL in single-dose pen or single-dose vial.

Learn more

Zepbound is a prescription medicine. For more information, call 1-800-LillyRx (1-800-545-5979) or go to **www.zepbound.lilly.com.**

This summary provides basic information about Zepbound but does not include all information known about this medicine. Read the information that comes with your prescription each time your prescription is filled. This information does not take the place of talking with your healthcare provider. Be sure to talk to your healthcare provider about Zepbound and how to take it. Your healthcare provider is the best person to help you decide if Zepbound is right for you.

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About Lilly

Lilly is a medicine company turning science into healing to make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help tens of millions of people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges: redefining diabetes care; treating obesity and curtailing its most devastating long-term effects; advancing the fight against Alzheimer's disease; providing solutions to some of the most debilitating immune system disorders; and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit Lilly.com and Lilly.com/news, or follow us on Facebook, Instagram and LinkedIn. P-LLY

Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Zepbound (tirzepatide) as a potential treatment for adults with moderate-to-severe obstructive sleep apnea (OSA) and obesity and other milestones relating to Zepbound and its clinical trials, and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of drug research, development, and commercialization. Among other things, there is no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with study results to date, that Zepbound will receive additional regulatory approvals, or that Lilly will execute its strategy as expected. For further discussion of these and other risks and uncertainties that could cause actual results to differ from Lilly's expectations, see Lilly's Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

[1]Zepbound. Prescribing Information. Lilly USA, LLC.

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