

Wellness

08 23

INSIDE: A trendy anti-obesity drug



Weight Loss Game-Changer

In the seemingly never-ending quest for weight-loss treatments, one medication has stood out: semaglutide. Here's what you need to know.

BY CATHY CASSINOS-CARR

It wasn't the celebrity Tweets or the obnoxiously overplayed commercial jingle ("Oh, oh, oh, Ozempic") that prompted Kelly Thompson to give weight-loss injectables a try. It was social media stories from real people—people just like her.

"There was a gal I followed on Instagram who had lost 30 or 40 pounds, and one day she posted something like 'Thank God for this tool I found,' and I was like, 'Wait a minute,'" recalls Thompson (not her real name). A Folsom resident and working mom in her mid-40s, Thompson was tipping the scales at 200 pounds when her doctor referred her to a weight management program at Sutter Health, where she was prescribed Wegovy, the only semaglutide injectable currently FDA approved for weight loss.

Where phentermine, Jenny Craig, the keto diet and other methods have failed her, this stuff—plus scaling way back on the lasagna—works, she says. After just two months of a weekly Wegovy shot, Thompson dropped 20 pounds, with a goal of losing 15 to 20 more. "It's been absolutely life-changing for me," she says. The injection is no biggie, she says, even though it's self-administered.

It's not a magic bullet, and it's not for everyone. But Wegovy and its sister semaglutide injectable Ozempic—a diabetes drug not FDA approved for weight loss, but popularly used that way—are making headlines, and with good reason: For many, they work. In a landmark study published in *The New England Journal of Medicine*, people with obesity who used 2.4 mg of injectable semaglutide weekly in combination with lifestyle interventions lost nearly 15 percent of their body weight, averaging 34 pounds.

Could this drug be a game-changer in the fight against obesity, which affects more than 100 million Americans and is linked to nearly every life-threatening condition you can name?

Maybe. But as local experts interviewed for this story shared, questions hover—like, is it safe to take this medication forever?—and shortages have been a nightmare, especially for patients with diabetes who critically need the medication.

OH, OH, OH INDEED—The short story on injectable semaglutide goes like this: In December 2017, Ozempic was FDA approved to lower blood sugar levels in

adults with Type 2 diabetes. In 2021 came Wegovy, approved for weight loss for people with obesity or who are overweight with a comorbidity, such as high blood pressure. The two drugs are exactly the same, with one key difference: Wegovy boasts a higher dose of semaglutide, 2.4 mg; Ozempic's maximum is 2 mg.

While no one expected Ozempic to morph from diabetes drug to trendy weight loss product, the medication's fringe benefits didn't come as a surprise to Adeela Ansari, M.D., an endocrinologist with Dignity Health Mercy Medical Group in Elk Grove. "Historically when we've prescribed semaglutide, we've noticed that even though our primary intention was to get blood sugar under better control, the added benefit was weight loss," she says. In addition to the two injectables, semaglutide is available in pill form under the brand name Rybelsus, which is FDA approved to treat Type 2 diabetes.

Semaglutide's recent rise to fame may give it the sheen of a shooting star, but it's not a new drug, says Ansari. It's been nearly six years since Ozempic was introduced, and drugs in its classification—glucagon-like peptide-1 (GLP-1) receptor agonists—have been around even longer; the FDA approved the first of its class in 2005. How do they work? By mimicking the GLP-1 hormone released in the gut after eating, the medication signals the stomach to empty more slowly, creating a feeling of fullness and reducing appetite. It also prompts the pancreas to produce more insulin, reducing blood sugar (glucose).

Thompson says the medication also seems to quiet the mind, shutting off ob-

sessive thoughts about food. "I used to wake up in the morning thinking, 'What am I going to have for lunch today?'" she says. "You could say I have a food addiction. But this [medication] clears the noise out of my head about food and cravings so I can focus on healthy eating. Instead of wanting mashed potatoes with my chicken, I'm wanting vegetables. Who is this person?"

How the drug affects the brain is a bit of a mystery, says Mohamed Ali, M.D., who has spent some 20 years trying to unravel such things. Along with being chief of foregut, metabolic and general surgery at UC Davis Health, Ali is executive director of its Center for Alimentary and Metabolic Sciences, where scientists study the underlying factors that affect metabolic health.

"There's no reason why a drug that works on the digestive system should be informing someone's brain, right?" he says. "To me, the biggest revelation here is that by targeting the gastrointestinal system, you actually affect behavior. And that's fascinating."

Targeting the GI system can also wreak havoc in the form of side effects such as nausea, vomiting, diarrhea, constipation, bloating and abdominal discomfort. Thompson says she's one of the lucky ones, with only a few brief bouts of nausea that lasted "maybe five minutes." Not everyone is so lucky, but her experience may not be uncommon: Preliminary studies suggest most side effects are mild to moderate in severity, and transient. "Every patient responds differently," says Anthony Huynh, D.O., a weight-management specialist

with Sutter Medical Group in Sacramento. But most tolerate semaglutide well, he says, especially at lower doses.

Less tolerable for many is the exorbitant cost of the drug when insurance won't cover it—a common plight for those who don't meet patient criteria.

INSURANCE, SHORTAGES AND OTHER STICKY WICKETS—For individuals who qualify for Wegovy or Ozempic, the cost is about the same, says Huynh—typically anywhere from \$25 to \$100 a month, depending on deductible. But things get stickier when prescribing Ozempic off-label for weight loss. “It is possible to prescribe Ozempic for nondiabetics who have obesity, but because it's off-label it's paid out of pocket,” Huynh explains. Out-of-pocket costs for Ozempic run more than \$1,000 a month, says Huynh, but some are willing to pay it.

Consumers unable to obtain the drug through traditional channels are finding other potentially risky avenues, including online marketplaces and private clinics. Compounding pharmacies offering semaglutide at cheaper prices are another common source. But such cost-cutting measures may come at a price. In May, the FDA said it had received reports of adverse events from consumers who used compounded forms of semaglutide, whose formulations may be different from the FDA-approved version and potentially unsafe.

Overwhelming demand for the drug has led to critical shortages, curtailing supply to patients whose very survival may depend on it. “It's been a nightmare,” says Dignity Health's Ansari. For three months last year, she says, she and other doctors struggled to obtain the medication for longtime patients whose diabetes had been in check for years. “Keep in mind this is a patient population that are at risk of the kinds of uncontrolled complications that can happen if they don't get their medications,” she says. As of June, Ozempic and Wegovy both remained on the FDA's list of drug shortages.

STOP THE MEDICATION, REGAIN THE WEIGHT?—Supply and demand issues wax and wane. But for those using sema-

glutide for weight loss specifically, one overarching concern persists: sustainability. What happens when the medication is stopped? Do the pounds just pile back on?

Pretty much, say local experts, who have seen how this movie ends with other weight-loss drugs. “We know the minute they stop the medication and no longer have the help with appetite suppression, they will gain the weight back,” Huynh says.

Early research suggests the same. According to a large-scale study published last year in the journal *Diabetes, Obesity and Metabolism*, participants who stopped semaglutide and adjunct lifestyle interventions regained two-thirds of their weight loss within a year.

For UC Davis' Ali, such findings prompt a larger question. “If the disease comes back when people stop treatment,” he asks, “what's the point of that treatment?”

That's not to suggest throwing the baby out with the bathwater. “Just because a treatment is imperfect doesn't mean that you don't use it,” he says. “It may be the best you have at the time.”

But being effective in the short term and durable in the long-term are two different things, cautions Ali.

What will happen down the road to the thousands of people now using it?

Thompson hasn't been using Wegovy long, but she's already pondering that question. “That's the part I don't know yet,” she says. “What

happens when I get to my goal weight and want to go off these meds?”

The last thing she wants, she says, is to lose all that weight only to put it right back on.

MORE THAN WILLPOWER—The notion that people like Thompson shouldn't need medications at all, that willpower alone should do the trick, should be checked at the door, says Ali.

Obesity is a complex disease, he says, and science is still trying to understand it.

“I believe the biggest gap in treating obesity in 2023 is that we don't really understand the disease itself,” he says.

Not everyone will lose weight by simply eating less and exercising more, he says, because everyone is different.

“There is no disease that we would ever think is the same disease for everybody, yet we think of obesity that way,” he says. Lack of understanding about the disease leads to misjudgments about treatment, he says, and also leads to stigma.

LIFESTYLE INTERVENTIONS KEY—Experts emphasize that patients who use semaglutide or any other obesity treatment also need to do the work. Adopting healthy eating habits, increasing physical activity, behavior modification—all are necessary for success, they say, not just for weight loss, but to improve health overall.

Doctors call these “lifestyle interventions.” It's not a new message.

Thompson, who is eating more salads these days, says she's clear on that. “If you don't do the work, if you continue to eat doughnuts and cookies all day, medications alone are not going to help,” she says. Sutter's weight management program helps to keep her in check, she says, with a team of experts to guide her, plus monthly appointments and medical monitoring to ensure she's staying healthy and on course.

NOT FOR EVERYONE—Semaglutide is not for everyone, and doctors need to exercise caution when prescribing it, Ansari says. The most prudent approach, she suggests, is reserving it for those who are prediabetic or predisposed to other weight-related conditions—not those who just want to shed a few pounds.

Even aspirin or other seemingly benign OTC drugs can have side effects, she says, so doctors prescribing semaglutide need to be sure benefit outweighs risk, especially when the product is in short supply.

Whether it's safe to use long term is still unknown. Experts aren't yet seeing any serious side effects from its continued use, Ansari says. But only time will tell.

“My gut feeling is that we'll find out you can't stay on this medication forever,” says Ali. While it can be a “great option and very effective” for the short term, he says, lasting success is harder to come by—so patients are advised to put a long-range plan in place. **S**

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