



GLP-1 receptor agonists: Breaking down the hype and demand

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For pharmacists like Candis Morello who are treating patients using GLP-1 receptor agonists, it's been a challenging few months navigating the shortage of this class of medications.

"This particular class of drugs is in such high demand right now; I don't think manufacturers expected this outcome," said Morello, PharmD, APh, CDCES, FCSHP, FASHP, a professor of clinical pharmacy at the University of California San Diego Skaggs School of Pharmacy and Pharmaceutical Sciences.

Morello said that because of GLP-1 receptor agonist drug shortages, she's been unable to initiate new starts or increase a patient's dose for the last several months.

"I've had to delay initiation or delay titration in my patients. I start them off with a lower dose and can only use the lower doses," said Morello, who is a clinical pharmacist and director of the Diabetes Intense Medical Management

Clinic at the Veterans Affairs San Diego Healthcare System.

Because the drugs are so highly effective, the American Diabetes Association now recommends GLP-1 receptor agonists as a first injectable over insulin for the majority of patients with type 2 diabetes.

In addition to being effective diabetes medications, GLP-1 drugs have demonstrated superior weight loss results for obesity. A March 2021 study published in *NEJM* found that adults using 2.4 mg of semaglutide lost an average of 35 pounds, or 15% of their body weight, within 15 months. The medications mimic the hormones that the intestines produce when eating, and together with a relatively safe adverse effect profile, have made this

third generation of medication attractive compared with older drugs for those wishing to lose weight.

"Shortages are also happening because of social media," said Jennifer Goldman, PharmD, CDCES, BC-ADM, FCCP, a professor of pharmacy practice at Massachusetts College of Pharmacy and Health Sciences and a clinical pharmacist at Well Life. She said the social media platform TikTok has dedicated pages for the use of these drugs for weight loss.

Like Morello, Goldman has had to keep her patients on lower doses of GLP-1 receptor agonists for the time being.

"A lower dose temporarily is not a bad thing," she said. "Work with the doses available—you can go up and down—these drugs are safe and don't cause low blood glucose reactions, typically. Plus, the differences between the doses are small."

Evidence

In 2021, FDA approved Wegovy semaglutide (Novo Nordisk) for weight loss. Ozempic (Novo Nordisk), which was approved 4 years earlier for type 2

diabetes, also contains semaglutide, but at a higher dose—2.4 mg—than Wegovy.

Although GLP-1 receptor agonist medications have existed since 2005 with exenatide (Byetta—AstraZeneca) and liraglutide (Victoza, Saxenda—Novo Nordisk) for patients with type 2 diabetes, the Cleveland Clinic noted on their Health Essentials blog that newer, longer-acting once-weekly GLP-1 receptor agonist medications like dulaglutide (Trulicity—Eli Lilly) have appeared to be more effective in treating obesity and lowering blood glucose.

In addition to the GLP-1 receptor agonists, FDA recently approved a GIP/GLP-1 receptor agonist combination called tirzepatide (Mounjaro—Eli Lilly) for people with type 2 diabetes. This weekly injection has also become popular for weight loss—outcomes of studies showed patients experienced up to 25% of body weight loss on tirzepatide.

In general, evidence from clinical trials with GLP-1 receptor agonists demonstrated safety and efficacy of controlling patient's glucose, but also have shown multiple benefits of reducing weight and improving cardiovascular health, according to Morello. "Especially for someone with type 2 diabetes, if you can protect the heart and reduce weight, the benefits are all encompassing and positive outcomes can be achieved with diabetes and associated comorbidities."

On average, people with type 2 diabetes have twice the risk of cardiovascular disease as people without diabetes.

Cost

One major barrier to patients accessing GLP-1 receptor agonists medications is cost. The subcutaneous, weekly injections list for around \$1,200 per month for one dose. Higher doses will cost more, and insurance coverage can also be limited.

Most patients use manufacturer coupon cards to purchase GLP-1 receptor agonists. "There are coupons available for the lower doses, which can give pharmacists time to work with the provider to place a prior authorization request for use with the insurance company," said Morello.

Providers can prescribe these medications off-label for patients who need to lose weight, but Goldman points out the tricky position pharmacists might find themselves in when patients use coupon cards.

"What happens on the pharmacy end if a pharmacist fills it for obesity and it's not indicated for that? Is someone going to come back and recoup that money?" said Goldman. "If a pharmacist has to check a box saying the patient has diabetes to have the savings card—that puts them in the middle. They can call the provider, but the provider can say they can write the prescription for whatever they want." She said the demand for these medications also highlights how desperate people with obesity are for effective treatment.

"One of the things I've seen particularly coming into 2023 is that many insurance companies are starting to require [diabetes] diagnosis before they will approve," said Theresa Tolle, BPharm, FAPhA, 2022–2023 APhA president and owner of Bay Street Pharmacy in Sebastian, FL, during a January 2023 APhA webinar on drug shortages.

Rarely will an insurer cover a GLP-1 receptor agonist for weight loss purposes. In addition, manufacturers have tightened access amidst the shortages. In early 2023, it was reported that Eli Lilly was limiting tirzepatide for only those patients with type 2 diabetes.

Pharmacists' role

"As the complexity of drugs increases and patient's comorbidities increase, these are all areas of opportunities for a pharmacist's knowledge and skill sets to help patients," said Morello.

According to the Cleveland Clinic, GLP-1 receptor agonists don't have as many adverse effects as other diabetes medications. Because they work

by stimulating hormones in a person's gut, the most common adverse effects are limited to digestion and can include abdominal pain, constipation, diarrhea, and nausea.

For patients with type 2 diabetes taking these medications, pharmacists should also be aware of the risk of a patient's blood glucose levels going too low, especially when they are used in combination with other diabetes medications such as insulin or sulfonylureas.



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Morello said pharmacists also need to remember the importance of counseling. "I tell patients we want to access your motivation—it's not just a drug that will help you lose weight," she said. "These drugs work well, but they need to be coupled with long term lifestyle changes."

"We have to look at the whole picture and take a holistic approach. GLP-1s are good for heart health, weight loss, kidney protection, and diabetes, but I never want us to lose sight of educating on the importance of a healthy diet and regular physical activity," said Morello. "When pharmacists provide counseling on these drugs, we need to include these other components. All of these efforts combined can produce astounding results." ■