How Do GLP-1 Receptor Agonists, Like Ozempic or Mounjaro, Work?

Our easy-to-read fact sheets provide clinicians with reliable information to share with patients and their caregivers.

Glucagon-like peptide-1 (GLP-1) is a hormone released when food is eaten to slow gastric emptying, the process by which food leaves the stomach, so that the body can absorb nutrients from food. It also increases insulin release from the pancreas and controls the feeling of satiety after eating.[1]

Insulin is a hormone produced by the pancreas that regulates the amount of glucose in the blood. When food is eaten, blood sugar increases, thus signaling the incretin system to release insulin. In some conditions, such as obesity and diabetes, the body does not respond to nutrients properly, which leads to the incretin system not functioning correctly and an increase in blood sugar.[2]

GLP-1 receptor agonists mimic the body's production of GLP-1 and are approved to treat patients with obesity and type 2 diabetes.[1]

GLP-1 receptor agonists approved for use among patients with type 2 diabetes include dulaglutide (Trulicity®), exenatide (Bydureon BCise®, Byetta®), liraglutide (Victoza®), insulin glargine/lixisenatide (Soliqua 100/33®), semaglutide (Ozempic®, Rybelsus®), and most recently, tirzepatide (Mounjaro®).

GLP-1 receptor agonists approved for chronic weight management among patients who have obesity or overweight and other weight-related conditions — including hypertension, type 2 diabetes, or obstructive sleep apnea — include liraglutide (Saxenda®), semaglutide (Wegovy®), and most recently, tirzepatide (Zepbound®).

How Do GLP-1 Receptor Agonists Work?

GLP-1 receptor agonists activate the GLP-1 receptors located in the hypothalamus in the brain, which regulates food intake. By activating these receptors, GLP-1 receptor agonists decrease the feeling of hunger and causes the patient to eat less. GLP-1 receptor agonists also bind to the GLP-1 receptors on certain neurons in the brain to decrease hunger and increase satiety. They have been shown to slow gastric emptying within the first hour of eating, resulting in the feeling of being full. Patients who use GLP-1 receptor agonists experience reduced appetite and hunger, lower preference for high calorie foods, decrease in food cravings, and better overall control of their eating habits.[3]

After weight loss, the body may compensate by lowering the amount of circulatory weight regulating hormones, such as leptin. GLP-1 receptor agonists contribute to weight loss maintenance by reducing the compensatory decrease of leptin in the body.[3]

GLP-1 Receptor Agonists in Patients With Diabetes

GLP-1 receptor agonists are approved to treat patients with type 2 diabetes. Among these patients, the body both decreases insulin release and develops a resistance to already-released insulin, resulting in a decreased production of GLP-1 receptors.[2]

Among patients with type 2 diabetes, GLP-1 receptor agonists have many effects, such as improving insulin sensitivity, decreasing glycated hemoglobin (HbA_{1c}) levels, slowing gastric emptying, increasing fullness, decreasing free fatty acid concentrations, and decreasing body weight. These medications also increase the GLP-1 receptors produced by the body.[2]

For patients with type 2 diabetes, GLP-1 receptor agonist treatment options include:

- Once-weekly dulaglutide (subcutaneous injection; Trulicity®);
- Twice-daily exenatide before meals (subcutaneous injection; Byetta®);
- Once-weekly exenatide (subcutaneous injection; Bydureon BCise®);
- Once-daily liraglutide (subcutaneous injection; Victoza®);
- Once-daily insulin glargine/lixisenatide (subcutaneous injection; Soliqua 100/33®);
- Once-weekly semaglutide (subcutaneous injection; Ozempic®);
- Once-daily semaglutide (oral; Rybelsus®); and,
- Once-weekly tirzepatide (subcutaneous injection; Mounjaro®).

GLP-1 Receptor Agonists in Patients With Obesity or Overweight

Obesity is defined as a body mass index (BMI) of 30 kg/m^2 or higher, whereas overweight is defined as a BMI of 25 kg/m^2 to 29.9 kg/m^2. GLP-1 receptor agonists approved for weight loss or weight management are subcutaneous injections. Treatment options include daily liraglutide (Saxenda®), once-weekly semaglutide (Wegovy®), and once-weekly tirzepatide (Zepbound®).[4]

These GLP-1 receptor agonists are approved for patients with obesity and for those with a BMI greater than 27 kg/m^2 who are also diagnosed with weight-related conditions, such as hypertension, dyslipidemia, type 2 diabetes, obstructive sleep apnea, or cardiovascular disease.

GLP-1 receptor agonists have a beneficial role in the management obesity, as the condition impairs GLP-1 secretions in the gut. Among this patient population, GLP-1 receptor agonists reduce appetite and, thus, reduce food intake, leading to long-term weight loss. The nausea and vomiting may occur as side effects of usage and do not significantly affect weight loss.[4]

Side Effects of GLP-1 Receptor Agonists

Because of the slow gastric emptying, these medications can cause gastrointestinal issues, including nausea, diarrhea, and vomiting. These adverse events mostly occur following a change in dose. Gradually increasing the dose has been shown to improve these side effects.[1,5] Other side effects include hypoglycemia and ketoacidosis.[1,5]

These medications are also known to cause more serious side effects, such as acute pancreatitis and gallbladder disease.[3,5] Some studies have shown links between GLP-1 receptor agonist use and risks for thyroid cancer and suicidal ideation, but these findings are not conclusive.[4]

Frequently Asked Questions

What are the side effects of GLP-1 receptor agonists?

GLP-1 receptor agonists can cause gastrointestinal side effects, such as nausea and vomiting. If this occurs, you should contact your provider, as you may need a lower dose of the medication. Your provider may recommend slowing the titration process, which could mean waiting longer than 4 weeks before increasing the dose of the medication to prevent nausea and vomiting.[1]

GLP-1 receptor agonists may cause injection site reactions. It is recommended to use a different injection site with each dose by rotating between the abdomen, thigh, or upper arm.[4]

Use of GLP-1 receptor agonists has also been associated with more severe side effects such as gallbladder issues like cholelithiasis, cholecystitis, and acute pancreatitis. However, these events are rare and require further research. [4,5]

Do GLP-1 receptor agonists interact with other medications?

Among patients with type 2 diabetes, use of GLP-1 receptor agonists with other blood sugar-lowering medications, such as sulfonylureas and insulin, may increase the chance of hypoglycemia.[6,7]

Other medications such as combined birth control, acetaminophen, digoxin (Lanoxin®), and warfarin have decreased absorption when used with GLP-1 receptor agonists. Studies have shown that this reduction did not cause a decrease in the effect of the medication. However, it is recommended to take birth control and acetaminophen at least 1 hour before the GLP-1 receptor agonist. Patients receiving warfarin should frequently monitor their international normalized ratio (INR). [6,7]

It is recommended to tell your physician about the medications you are taking before starting a GLP-1 receptor agonist. When taken with short-acting insulin or sulfonylureas, GLP-1 receptor agonists can increase your risk for low blood sugar.[7]

How long do GLP-1 receptor agonists stay in the body?

GLP-1 receptor agonists that are prescribed once weekly, such as semaglutide, dulaglutide, and long-acting release exenatide, are inactive and half-way eliminated in 5 to 7 days. Once-daily exenatide and lixisenatide are inactive and half-way eliminated in about 2.5 to 3 hours.[5]

What happens if I stop taking a GLP-1 receptor agonist?

The fat lost while taking GLP-1 receptor agonists is often gained back when the medication is stopped. The benefits to blood sugar levels are also often lost. In one study, patients who stopped liraglutide had a 70% gain in fat after 1 year. The study also found that patients who continued to exercise maintained weight loss post-treatment. Talk with your doctor about the best way to stop taking these medications.[8]