



GLP1s: Tirzepatide and Semaglutide

Tirzepatide (Mounjaro®), is the newest approval in a class of medications known as GLP1 agonists (glucagon-like peptide-1 agonists). This is a medication originally developed to treat diabetes but is more and more commonly being used for weight loss. Semaglutide (Ozempic®/ Wegovy®) is an earlier GLP1; Ozempic® is FDA (Food & Drug Administration) approved for the treatment of diabetes, Wegovy® - the same medication but higher dose - is approved for weight loss. Although tirzepatide is currently branded only for diabetes, like Wegovy® we use it almost exclusively for its metabolic and weight loss benefits.

GLP1 is a peptide hormone secreted by your gut. Tirzepatide differs from semaglutide in that it contains a second peptide called GIP (glucose-dependent insulinotropic polypeptide), a peptide also secreted by the gut, just in a different spot. What makes these medications interesting for weight loss, is their net effect on the production of insulin - a central hormone in fat storage regulation.

Insulin is the hormone made by your pancreas to tell your body what to do with the food you eat. The instructions from insulin are to either "use it" or "store it," depending on if you need food for fuel right now or not. Directed by insulin, unused fuel gets stored for later - in a fat cell, typically in your midsection.

Insulin is a fat storage hormone. If you have too much insulin in circulation (insulin resistance), you likely have too much excess fuel stored as fat.

Through a complex series of pathways, both tirzepatide and semaglutide do two important things; improve insulin receptor sensitivity, and over time, suppress insulin production. The end result is better blood sugar control and loss of extra central fat stores. Things to know about these peptides:

- **Semaglutide** has formal FDA indication for treating both diabetes and weight loss but only in a subset of obese patients with comorbidities like hypertension, who have failed other (less expensive) weight loss medications.
- **Tirzepatide** only has FDA indication for treating diabetes - using this peptide for weight loss is strongly supported by clinical trial data, but currently considered 'off label.'

- Both peptides are administered in a once weekly subcutaneous injection.
- Both peptides have extremely positive effects on other cardiometabolic markers (cholesterol, inflammation), liver function, and risk of heart disease.
- Both peptides are safe for short- and long-term use.
- Tizepatide is superior to semaglutide; it produces better blood sugar control, more weight loss, and has fewer side effects.
- Results are dose dependent i.e., higher doses produce more weight loss.

Off-label prescribing is when a physician gives you a drug that the U.S. Food and Drug Administration (FDA) has approved to treat a condition different than your condition. This practice is legal and common. One in five prescriptions written today are for off-label use. **Insurance companies will not, under any circumstance, approve coverage of an expensive medication for off-label use.*

How Do They Work? Here's What We Know:

GLP1s

- Suppresses glucagon secretion which lowers blood sugar.
- Decreases appetite by slowing transit through the stomach.
- Improves insulin receptor sensitivity.
- Restores youthful metabolic function.

GIPs

- Suppresses glucagon secretion which lowers blood sugar.
- Decreases appetite through neuronal modulation.
- Protects lean muscle mass.
- Improves lipid metabolism & cardiovascular risk.

How these peptides work for blood sugar control seems straightforward. How they work so efficiently for weight loss is not as clear. Both decrease appetite but decreased caloric intake alone does not explain the weight loss. GLP1 secretion improves glucose metabolism but by some *mechanism, it must improve long-term insulin receptor sensitivity as well.*

This class of peptides is generally well tolerated by patients with and without diabetes. Side effects are typically limited to nausea and constipation/diarrhea but can include the following:

Possible Side Effects

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|--------------------|------------------------|
| • Loss of appetite | • Confusion |
| • Nausea | • Dizziness |
| • Diarrhea | • Drowsiness |
| • Constipation | • Headache |
| • Anxiety | • Increased heart rate |
| • Blurred vision | |

Will This Be Covered By My Insurance?

Short answer: Probably not – unless you have diabetes, obesity complicated by other medical conditions, or have insurance that does not require prior authorization.

Insurance companies only pay for branded medications which are FDA indicated for specific medical conditions. Your insurance company gets to choose these medications. Insurance typically only offers coverage for medications FDA approved for the medical condition it is being prescribed for. Tirzepatide is FDA approved for the treatment of type 2 diabetes. If you have diabetes, your insurance may provide coverage for this medication. If you are prescribed tirzepatide for an 'off label' use, like insulin resistance, prediabetes, or weight loss, your insurance is not obligated to, and will likely not, help cover the cost of this medication. Semaglutide is FDA approved for weight loss, but only in selected patient populations.

Without insurance assistance, these medications are very expensive. Under specific circumstances, some compounding pharmacies can compound these medications at a lower cost.

How Long Do I Take This Medication?

Great question. How long did it take for you to become insulin resistant or overweight in the first place? It is impossible to answer either question, but the answer is likely the same. One year? 5 years? 20 years? We are all unique. Some patients use these medications for a couple of months, others for longer periods of time. Regardless of your individual situation, they are safe for both short- and long-term use. You and your health care provider will determine what course of treatment is appropriate for you. Who should not take these medications?

- Patients who have had an allergic reaction to tirzepatide or semaglutide in the past, or any of the other GLP1s.
- Patients with a history of thyroid cancer.
- Patients who should not lose weight or who already have a low body mass index

Dosing/Ordering/Follow up For Tirzepatide:

- Our office can order/ship to you compounded tirzepatide which comes in vials that contain 200 units (33.2mg, 2ml).
- Dosing starts with 15 units weekly (2.5mg) and is increased by 15 units every 4 weeks up to a maximum of 90 units weekly (15mg) per individual patient need.

- If you are using a dose of 45 units weekly, then 1 vial will last 4.44 weeks. Because of processing and shipping times, it is best to order 2 vials at a time if you are using this dose or anything higher to avoid lapses in treatment.
- **All patients of Lindgren Functional Medicine using any injectable weight loss medications (*Mounjaro, Tirzepatide, Ozempic, Victoza, Semaglutide, etc.*) are REQUIRED to have a weight and blood pressure check by a clinical staff member or provide proper signed documentation from their General Practitioner EVERY THREE MONTHS. (*Typically, every 4 weeks when patients are first getting started.*)**

Dosing/Ordering/Follow up For Semaglutide:

- Our office can order/ship to you compounded semaglutide which comes in two separate vials that contain a total of 200 units (10mg, 1ml in each vial).
- Dosing is started at 5 units (0.25mg) weekly and increased by 5 units every 2-4 weeks up to a maximum of 50 units weekly (2.5mg) per individual patient need.
- If you are using a dose of 50 units weekly, 1 vial will last exactly 4 weeks. Because of processing and shipping times, it is best to order 2 vials at a time if you are using this dose to avoid lapses in treatment.

Tips

- Peptides are fragile! They are sensitive to heat, aggressive shaking, and UV light. They are stored in dark glass vials and will arrive on ice. Your peptides should be promptly opened and refrigerated. Be careful not to drop or shake them.
- Tirzepatide and semaglutide are administered via a small subcutaneous injection once weekly. Side effects are reported to be less pronounced if the injection is given under the skin on the leg versus in the abdomen.
- Temporary injection site itching is common.
- We are happy to schedule an injection teaching appointment with one of our staff members to make sure you are comfortable injecting. Please call the desk when your peptides arrive to schedule this.
- Side effects can and do occur but should be mild and self-limited. Do not increase your dose if you are having side effects at your current dose. Call the office if you have questions or concerns about potential side effects.