

Semaglutide is in a class of medications called glucagon-like peptide 1 (GLP-1) agonists or incretin mimetics. GLP-1 agonists work by stimulating your pancreas to produce right dose of insulin in response to the level of blood glucose. Semaglutide causes the stomach to empty over a longer period of time. The idea of the stomach processing food more slowly can seem counterintuitive to patients. The slow and consistent digestion is an early step in the chain reaction that makes semaglutide an effective weight loss drug. When the stomach takes more time to empty itself of food, it sends signals of “fullness” to the brain. The result of this process is a powerful appetite suppression effect based on the patient’s own natural insulin production. This means patients can benefit from medically assisted weight loss without any need for invasive surgeries or harsh stimulants.

A semaglutide regimen will also lead to healthier blood sugar levels, which can help patients feel more energetic throughout their day. Stabilized and controlled blood sugar levels can also help improve other areas of overall health.

During the increase in dosage, patients should be aware of any unwanted side effects such as:

- Loss of appetite (i.e., constant feelings of fullness that go beyond the desired results)
- Light-headed or dizzy sensations
- Persistent lethargic feeling
- Gastrointestinal discomfort
- Diarrhea

There is an impressive body of scientific evidence backing semaglutide’s effectiveness as a weight-loss drug. Some of the research that was conducted leading up to its recent FDA approval for weight management includes:

- A randomized, double-blind trial occurring over a long period in the mid-2010s found that semaglutide use resulted in significant body weight reductions. This weight reduction was not only compared to a placebo group, but also compared to another substance in the GLP-1 receptor agonist class called Liraglutide.(1). O’Neil, P. M., Birkenfeld, A. L., McGowan, B., Mosenzon, O., Pedersen, S. D., Wharton, S., ... & Wilding, J. P. (2018). Efficacy and safety of semaglutide compared with liraglutide and placebo for weight loss in patients with obesity: a

randomised, double-blind, placebo and active controlled, doseranging, phase 2 trial. *The Lancet*, 392(10148), 637-

649. <https://www.sciencedirect.com/science/article/pii/S0140673618317732>

□ A 2019 report found that semaglutide “appears to be superior” for weight loss stimulation in type 2 diabetes patients when evaluated compared to a variety of other GLP-1 receptor agonists. The same study noted that trials evaluating semaglutide as a weight-loss drug exceeded the criterion set forth by both the FDA and EMA (European Medicines Agency) for obesity medications. This was regardless of whether the patients evaluated were Type 2 diabetics, and that it achieved these results with “no safety concerns”.(2) Christou, G. A., Katsiki, N., Blundell, J., Fruhbeck, G., & Kiortsis, D. N. (2019).

Semaglutide as a promising antiobesity drug. *Obesity Reviews*, 20(6), 805-

815. <https://onlinelibrary.wiley.com/doi/abs/10.1111/obr.12839>

□ A more recent double-blind trial involved nearly 2,000 individuals who were not diagnosed with diabetes and had a BMI over 30. When individuals implemented other lifestyle changes such as exercise, this study found the mean change in body weight after 68 weeks of semaglutide treatment was -14.9%. The placebo group only saw a -2.4% change.(3) Wilding, J. P., Batterham, R. L., Calanna, S., Davies, M., Van Gaal, L. F., Lingvay, I., ... & Kushner, R. F. (2021). Once-weekly semaglutide in adults with overweight or obesity. *New England Journal of Medicine*. 384, 989-

1002. <https://www.nejm.org/doi/full/10.1056/NEJMoa2032183>

□ Another interesting study from 2020 concluded that semaglutide provides superior weight loss efficacy with no demonstrable link to “gastrointestinal adverse events.” Gastrointestinal adverse events included negative side effects in the stomach and digestive system, such as stomachaches and diarrhea.(4) Lingvay, I., Hansen, T., Macura, S., Marre, M., Nauck, M. A., De La Rosa, R., ... & Wilding, J. (2020). Superior weight loss with once-weekly semaglutide versus other glucagon-like peptide-1 receptor agonists is independent of gastrointestinal adverse events. *BMJ Open Diabetes Research and Care*, 8(2), e001706. <https://drc.bmj.com/content/8/2/>

□ Yet another study focusing on semaglutide and weight loss paired the substance (or, alternately, a placebo) with intensive behavioral therapy and a low-calorie diet. This study also concluded that semaglutide use resulted in demonstrably superior weight loss outcomes. (5) Wadden, T. A., Bailey, T. S., Billings, L. K., Davies, M., Frias, J. P., Koroleva, A., ... & STEP 3 Investigators. (2021). Effect of subcutaneous semaglutide vs placebo as an adjunct to intensive behavioral therapy on body weight in adults with overweight or obesity: the STEP 3 randomized clinical trial. *Jama*, 325(14), 1403-1413. https://jamanetwork.com/journals/jama/articleabstract/277702RxPad_WeightLoss.03.07.22.pdf