# SEMAGLUTIDE (OZEMPIC) A POTENT WEAPON IN THE FIGHT AGAINST OBESITY

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Obesity is a chronic, relapsing disease associated with multiple complications and a substantial morbidity, mortality and health care burden. Global prevalence of obesity has been on the rise for the past several decades, a trend predicted to continue. Lifestyle modification is the foundation of treatment for individuals with overweight or obesity, but typically achieves only modest weight loss that is often regained and challenging to maintain. Pharmacological treatments for obesity provide a valuable adjunct to lifestyle interventions, but until recently the available agents only offered moderate weight loss and came with treatment-limiting side effects.

The most promising of anti-obesity agents include glucagon-like peptide1 (GLP-1) receptor agonists, liraglutide (Saxenda) and semaglutide (Ozempic). GLP-1 agonists not only increase insulin release but also delay gastric emptying resulting in decreased oral intake and therefore culminating in weight loss. Liraglutide was the first GLP-1 agonist approved for obesity management and requires daily subcutaneous injections. Semaglutide (approved by Federal Drug Agency of USA in June, 2021) on the other hand is a weekly subcutaneous injection and has shown better weight loss outcomes than liraglutide. In a randomized controlled trial including 338 adults, after 68 weeks, participants in the semaglutide group lost more weight than the liraglutide group (-15.8 versus -6.4 percent).[1] Since its approval, semaglutide has seen an exponential increase in its global demand, has enjoyed widespread adoption and has acquired many titles including 'miracle drug', 'game-changer therapy' and is clearly the most promising weight-loss treatment in history.

Semaglutide has demonstrated efficacy in weight loss in trials involving patients with and without type 2 diabetes. In the United States, both oral and injectable preparations are approved for the treatment of type 2 diabetes, whereas only the injectable form is approved for the treatment of obesity. In STEP 1, a randomized controlled trial including 1961 adults without diabetes and a BMI of ≥30 kg/m², after 68 weeks of once-weekly subcutaneous 2.4 mg semaglutide, 15% weight loss was seen in treatment group as compared to 24% in placebo group.[2] Similar, results were seen in STEP 2 trial in diabetics.[3]

Semaglutide also seems to be cardio-protective which is a major benefit. It has shown to reduce major cardiovascular disease events in adults with type 2 diabetes and established cardiovascular disease or chronic kidney disease.[4]

Most common side effects of semaglutide are gastrointestinal as expected for any GLP-1 agonist. Mostly, these are transient and only rarely require treatment cessation. More serious adverse effects include pancreatitis and medullary thyroid carcinoma (animal studies).[5] Semaglutide should not be used in patients with history of pancreatitis, a personal or family history of medullary thyroid carcinoma or in patients with a rare condition called Multiple Endocrine Neoplasia syndrome type 2 (MEN 2).

The road ahead for semaglutide may not entirely be without bumps. The high cost remains a formidable challenge for its widespread adoption. There is dearth of longterm safety data. Newer medications in the pipeline could test its current dominance. Tirzepatide, a novel dual-acting GLP-1 and GIP (gastric inhibitory polypeptide) agonist is already showing better results than Semaglutide at 40 weeks of therapy.[6] The biggest challenge could be an oral GLP-1 agonist with similar or better efficacy. Orforglipron is such a drug currently undergoing phase II trials and showing promising results.[7] Until then, semaglutide remains a potent weapon against the obesity epidemic and could be a key drug in turning the tide.

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