

Comparing GLP-1 agonists: Efficacy, safety, and patient compliance.

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Introduction

Glucagon-like peptide-1 (GLP-1) receptor agonists have revolutionized the management of type 2 diabetes mellitus (T2DM) by improving glycemic control while offering additional benefits such as weight loss and cardiovascular protection. Since their introduction, several GLP-1 agonists have entered the market, each with unique pharmacokinetic profiles, dosing schedules, efficacy, safety considerations, and patient adherence factors. This mini article aims to compare the most commonly prescribed GLP-1 receptor agonists regarding their efficacy, safety, and patient compliance to provide a comprehensive understanding for clinicians and patients [1].

GLP-1 receptor agonists mimic the incretin hormone GLP-1, which enhances glucose-dependent insulin secretion, suppresses glucagon release, slows gastric emptying, and promotes satiety. These mechanisms collectively improve blood glucose control and contribute to weight reduction, a critical benefit in T2DM management. Commonly prescribed GLP-1 agonists include exenatide (immediate-release and extended-release), liraglutide, dulaglutide, semaglutide (injectable and oral forms), and lixisenatide. Their differences lie primarily in molecular structure, half-life, dosing frequency, and clinical outcomes.

Multiple head-to-head trials and meta-analyses consistently demonstrate semaglutide as one of the most potent GLP-1 agonists for glycemic control and weight loss. Semaglutide reduces HbA1c by approximately 1.5% to 1.8% and promotes

significant weight loss (up to 5-7 kg on average). Its long half-life allows for once-weekly dosing, improving convenience. Similar to semaglutide in dosing frequency (once weekly), dulaglutide shows robust HbA1c reductions of around 1.3% to 1.6% and moderate weight loss. Clinical trials also suggest cardiovascular benefits comparable to semaglutide [2].

Administered once daily, liraglutide has demonstrated HbA1c reductions of about 1.0% to 1.5% and weight loss benefits. It is also FDA-approved for weight management under higher doses. Available as a twice-daily immediate-release form and a once-weekly extended-release form, exenatide reduces HbA1c by about 0.8% to 1.4%, with less pronounced weight loss compared to semaglutide or liraglutide.

Nausea, vomiting, and diarrhea are the most common adverse effects, often transient and dose-dependent. Immediate-release exenatide and liraglutide are associated with a higher incidence of GI symptoms due to their shorter half-lives and peak plasma concentrations [3].

There have been concerns about pancreatitis with GLP-1 agonists, but current evidence does not conclusively show an increased risk. Still, caution is advised in patients with a history of pancreatitis. Rodent studies suggested a risk of medullary thyroid carcinoma, but no causal relationship has been established in humans. Nonetheless, GLP-1 agonists are contraindicated in patients with personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2.

Because GLP-1 agonists enhance glucose-dependent insulin secretion, they have a low risk of hypoglycemia unless combined with insulin or sulfonylureas [4].

Major trials (e.g., SUSTAIN, REWIND, LEADER) have shown cardiovascular benefits or neutrality with semaglutide, dulaglutide, and liraglutide, making them preferred agents in patients with established cardiovascular disease. Once-weekly formulations (semaglutide, dulaglutide, extended-release exenatide) tend to have higher compliance rates than daily injections (liraglutide, lixisenatide). Less frequent dosing reduces the burden on patients, which is particularly beneficial for those with needle anxiety or busy lifestyles.

The introduction of oral semaglutide offers an alternative for patients reluctant to use injections. However, the oral form requires strict adherence to fasting and water intake protocols, which may affect real-world compliance. Ease of use, needle size, and device design impact patient satisfaction. Dulaglutide's single-use, pre-filled pen is often praised for simplicity, while other devices vary in complexity. GI side effects, especially early in treatment, can reduce compliance. Slow titration and patient education can mitigate these effects [5].

Conclusion

GLP-1 receptor agonists represent a cornerstone in modern T2DM management, with semaglutide and

dulaglutide demonstrating superior efficacy and cardiovascular benefits. While safety profiles are broadly similar, individual patient factors such as history of pancreatitis or thyroid cancer should guide agent selection. From a compliance standpoint, once-weekly dosing and user-friendly devices promote adherence, and the emergence of oral semaglutide expands patient choice. Ultimately, individualized therapy considering efficacy, safety, and patient preference maximizes the benefits of GLP-1 agonists, improving glycemic control and quality of life in patients with T2DM.

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