

Compounded Semaglutide: Navigating Safety, Dosing, and Risks

Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist, is approved by the U.S. Food and Drug Administration (FDA) under three brand names: Ozempic®, Wegovy®, and Rybelsus®. Each formulation has unique indications, preparations, and dosages, necessitating careful consideration by prescribers, as well as adequate patient counseling on how to use these medications.

Semaglutide functions as a GLP-1 receptor agonist with a 94% structural homology to human GLP-1. It acts by enhancing glucose-dependent insulin secretion, slowing gastric emptying, and acting on hypothalamic GLP-1 receptors. This medication's multifaceted actions contribute to its efficacy in managing blood glucose levels and facilitating weight loss. Its long half-life (approximately one week) categorizes it as a "long-acting" GLP-1 receptor agonist. After a stark increase in popularity as a weight loss agent and ongoing drug shortages, unauthorized compounded semaglutide products began to appear from med spas, clinics, and online retailers. This presents safety concerns related to therapeutic errors, lack of FDA regulatory oversight, and unauthorized products that are available without a prescription.

Poison Centers and the FDA Adverse Event Reporting System (FAERS) have received numerous reports of 10-fold dosing errors stemming from compounded vials of semaglutide. These errors occur secondary to variability in dosing instructions, inconsistent vial sizes and concentrations, as well as powder preparations that require reconstitution to obtain the correct concentration. Cases of administering daily doses instead of weekly have also occurred. The most common clinical effects include nausea, vomiting, diarrhea, and food intolerance. Due to its long half-life, symptoms can persist for multiple days. Serious adverse effects include dehydration, electrolyte imbalances, and possibly hypoglycemia.

Two studies, one using data from the National Poison Data System (NPDS) and the other using exposure cases from one poison center, characterized GLP-1 agonist exposures. The majority of cases in both studies involved unintentional overdoses with semaglutide being the most common agent. Hypoglycemic events occurred in a subset of patients with a prevalence of 2.4% using national data and 3.8% using poison center data (*Clin Toxicol* 2025;1-4, *J Med Toxicol* 2024;20(2):193-204).

Unintentional dosing errors with GLP-1 agonists continue to occur. Patients may seek medical attention due to prolonged symptoms. Treatment is symptomatic and supportive and usually consists of intravenous fluids, antiemetics, and electrolyte repletion, but may require prolonged treatment including inpatient hospitalization for intravenous fluids. Since hypoglycemia may occur, monitoring blood glucose levels is warranted.

Healthcare providers should consider consulting a local poison control center at 1-800-222-1222 for treatment guidance and monitoring recommendations for semaglutide-related adverse events.



Did you know?

Poison Centers have seen a 1,500% increase in calls over a five-year span related to overdoses or side effects of injectable weight-loss drugs.

In 2019, Poison Centers managed 531 cases related to GLP-1 agonist exposures. By 2024, this number skyrocketed to 8,485 cases. This dramatic rise highlights the growing popularity of GLP-1 agonists such as semaglutide, particularly to aid in weight loss. The heightened demand has led to shortages, prompting some individuals to seek alternatives through online sources or compounding pharmacies.

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