



Letter to Editor

Onset and Relapse of Depressive Disorders Associated With Wegovy® For Weight Loss

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We are writing to highlight concerns regarding the potential psychiatric side effects associated with antidiabetic medications, specifically semaglutide and liraglutide, both GLP-1 (glucagon-like peptide-1) agonists, particularly in the context of weight loss therapy.

These drugs have recently been shown to be successful in achieving expected weight loss [1,2]. However, a recent issue has raised concerns. In July 2023, the EMA initiated an ongoing assessment regarding the risk of suicidal thoughts and self-harm associated with semaglutide (Ozempic®, Wegovy®) and liraglutide [1]. This followed the first report of three cases notified by the Icelandic Medicines Agency [3].

We report two concurring significant cases notified to our Pharmacovigilance Center of new and relapsing depressive disorders in patients shortly after starting semaglutide (Wegovy®) for weight-loss.

In the first case, a 41-year-old woman had been hospitalized for acute depressive syndrome. Since then, her symptoms have been stabilized with aripiprazole, oxazepam, zopiclone, lorazepam, and paroxetine. One year later (on June 19, 2023), she started Wegovy® 0.5mg weekly for weight management. However, ten days after her initial and only Wegovy® injection, she experienced a change in mood, leading her to seek psychiatric consultation. Her condition worsened, resulting in her admission to a psychiatric unit 11 days later, with a diagnosis of severe depressive relapse, necessitating the discontinuation of semaglutide treatment.

In the second case, a 67-year-old woman, who had successfully completed a one-year course of venlafaxine 75 mg/day for generalized anxiety disorder, discontinued her treatment in April 2023 and remained stable. On June 14, 2023, she started a weekly 0.5 mg dosage of Wegovy® to address her weight-related concerns, without subsequent dose increases. However, approximately six weeks after starting Wegovy®, she developed a depressive syndrome with suicidal ideation. Consequently, Wegovy® was ceased and her prior medication, venlafaxine LP at 37.5mg per day, was reintroduced leading to her improvement.

Both patients had no concomitant treatment associated with an increased risk of depressive episodes, nor did they report any substance addiction. The chronology of events strongly suggests a potential risk of depressive disorders associated with semaglutide treatment, especially in patients with pre-existing risk factors for depression. The Naranjo score indicates that the association was considered “Possible” in the first case and “Probable” in the second case.

Clinical trials [2,4] have not identified such a risk of depressive or suicidal disorders for semaglutide. However and quite surprisingly, patients with a psychiatric history were excluded from these studies [2,4] despite the well-documented higher risk of psychiatric comorbidities among the obese population [5].

A query conducted on the WHO pharmacovigilance database (Vigibase®), which is the largest worldwide database for reported drug side effects, revealed a total of 379 cases related to “Suicidal Behavior And Predisposition To Self-Harm” as well as “Depressed Mood Disorders And Disturbances” (High-Level Group Terms

or HGLTs, according to the MedDRA dictionary version 26.0) associated with semaglutide. When the query was narrowed down with Preferred Terms (PTs), significant signal detection was observed for “Suicidal Depression” (IC025 = 1.2), “Depressed Mood” (IC025 = 0.6), “Depressive Symptom” (IC025 = 0.2), and “Suicidal Ideation” (IC025 = 0.2).

Semaglutide reduces hunger, increases satiety, and lowers blood glucose levels by activating the GLP-1 receptor. These receptors are found in various tissues, including the brain, potentially leading to some brain side effects.

Due to the observed link between depressive/suicidal disorders and Wegovy® in reported cases, coupled with the absence of safety data regarding semaglutide in patients with psychiatric history and the lack of such information in its Summary of Product Characteristics, we emphasize the need for awareness. Patients with a history of depressive disorders or suicidal thoughts should avoid semaglutide for severe obesity treatment. If prescribed, these patients should receive close psychiatric monitoring.

We greatly appreciate your attention to this crucial matter. Sharing this information can contribute to ongoing discussions and research on potential side effects of antidiabetic drugs like semaglutide.

Conflict of Interest: The authors declare that they have no conflict of interest.

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