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# Semaglutide: A revolution in the treatment of obesity and prevention of cardiovascular disease

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**Abstract**

**Introduction and Objective:** Obesity represents a significant public health concern in the 21st century, with a substantial burden of disease attributable to its complications, including type 2 diabetes, hypertension, and cardiovascular disease. The objective of this review is to evaluate the efficacy and safety of semaglutide, a GLP-1 receptor agonist, in the treatment of obesity and its impact on cardiometabolic risk factors.

**The Review and Methods:** This review is based on an analysis of the scientific literature, including meta-analyses and clinical trials. The PubMed, Scopus and Web of Science databases were searched for publications up to 2023.

**Abridged Description of the State of Knowledge:** The efficacy of semaglutide in reducing body weight in patients with obesity is supported by evidence from clinical trials. Its mechanism of action includes the delay of gastric emptying and the reduction of hunger. The drug has been demonstrated to exert a beneficial effect on the lipid profile and blood pressure, thereby reducing the risk of cardiovascular disease. The adverse effects, which are primarily gastrointestinal in nature, are typically mild and resolve with treatment.

**Summary:** Semaglutide represents a promising therapeutic option for obese patients, offering an effective means of reducing body weight and improving cardiometabolic parameters. However, further studies are required to evaluate the long-term effects of this therapy and its application in different patient populations.

**Keywords:** Semaglutide, obesity, weight reduction, GLP-1, cardiometabolic risk factors, drug treatment.

## Introduction to Obesity and its Health Complications

Obesity represents one of the most significant health challenges of the 21st century, with implications for social and economic wellbeing on a global scale. As defined by the World Health Organisation (WHO), obesity is a condition characterised by the excessive accumulation of adipose tissue in the body, which can lead to a range of adverse health outcomes [1].

An individual with a body mass index (BMI) of 30 kg/m² or more is considered obese, while an individual with a BMI between 25 and 29.9 kg/m² is considered overweight [2]. Obesity is associated with a number of serious medical conditions, including type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease, and various forms of cancer [3]. A substantial body of research indicates that being overweight is a major contributor to premature mortality [4]. Its adverse health effects have a detrimental impact on the quality of life and social functioning of individuals [5]. Despite the implementation of a plethora of educational initiatives and efforts to promote healthy lifestyles, the prevalence of obesity continues to increase, thereby rendering it a significant public health concern [6]. Notwithstanding the efficacy of traditional treatments, such as dietary modification and regular physical activity, these approaches often fail to produce lasting results [7]. Considering these challenges, pharmacotherapies that facilitate weight loss and weight management are assuming an increasingly critical role [16]. The advent of contemporary pharmaceuticals, exemplified by semaglutide, has marked the beginning of a new era of therapeutic possibilities in the management of obesity, offering patients more efficacious tools in the fight against excess body weight [8]. Semaglutide, which acts as a GLP-1 receptor agonist, has been demonstrated to promote weight loss and to have beneficial effects on cardiovascular risk factors [9]. Consequently, it represents an attractive therapeutic option for obese patients . In light of the mounting obesity epidemic, it is imperative to gain a deeper understanding of effective treatment strategies and implement them in a systematic manner to enhance public health outcomes [10].

## Mechanism of action of semaglutide in the context of weight reduction

Semaglutide, a glucagon-like peptide 1 (GLP-1) receptor agonist, plays a crucial role in body weight regulation through a multitude of physiological mechanisms [6]. GLP-1 is an incretin hormone that is naturally secreted in the gut in response to the ingestion of food. Its principal functions include the stimulation of insulin secretion, the inhibition of glucagon secretion, the delay of gastric emptying, and the reduction of appetite [6][8]. Semaglutide, which mimics the action of natural GLP-1, binds to GLP-1 receptors in the brain, particularly in areas responsible for the regulation of hunger and satiety [7]. This binding leads to a reduction in the feeling of hunger and an increase in the feeling of satiety [7]. One of the primary mechanisms through which semaglutide contributes to weight loss is by delaying gastric emptying [8]. The prolongation of the gastric residence time of food content results in a slower release of glucose into the blood, which reduces postprandial blood sugar spikes and mitigates the sensation of hunger after a meal [8]. This delay also leads to a reduction in food intake, which is a crucial aspect of weight loss [8]. By reducing the activity of neurons involved in hunger and increasing the activity of those involved in satiety, this drug has been shown to lead to a significant reduction in calorie intake [7].

In addition, semaglutide has the potential to influence food preferences, thereby reducing cravings for high-calorie, high-fat, and high-sugar foods, which may contribute to additional weight loss [9]. In addition, semaglutide has a longer half-life than other GLP-1 agonists, such as liraglutide, allowing once-weekly dosing [11]. This improves convenience and compliance, which is critical in the long-term treatment of obesity [11]. Because of its complex mechanism of action, semaglutide is a promising therapeutic option for patients with overweight [5].

**Comparison of semaglutide with other anti-obesity drugs**

Semaglutide, an innovative GLP-1 receptor agonist, shows superior efficacy and a favourable safety profile compared to other drugs used in the treatment of obesity [9]. Compared with other GLP-1 agonists, such as liraglutide, semaglutide has shown superior efficacy in weight loss, as evidenced by the results of numerous clinical trials [9][18]. Liraglutide, available at a dose of 3 mg per day, is also used in the therapy of obesity, but its weight loss efficacy is inferior to that of semaglutide, which is administered once weekly at a dose of 2.4 mg [14]. Semaglutide provides better and more sustained results, making it the preferred treatment option for many patients [9]. In comparison to liraglutide, semaglutide, administered on a weekly basis, has been demonstrated to result in greater weight loss, as evidenced by the findings of studies[9][18]. This discrepancy may potentially be attributed to the differing effects on energy intake regulation. This discrepancy may be due to the longer half-life of semaglutide, which allows blood levels to remain stable throughout the week, resulting in more effective appetite suppression and glycaemic control [10]. In addition, semaglutide is more convenient for patients due to its once-weekly dosing, which may lead to improved adherence [10]. It would also be useful to compare semaglutide with other anti-obesity drugs such as orlistat or fentermine-topiramate. Orlistat works by inhibiting intestinal fat absorption, leading to fat excretion. However, it is often associated with gastrointestinal side effects that limit its use [12]. Although fentermine-topiramate is an effective weight loss drug, it can cause serious adverse effects, including increased blood pressure and an increased risk of psychiatric disorders [16][17]. As a result, its use is usually limited to short-term interventions [16]. Compared with the traditional options mentioned above, semaglutide has a balanced efficacy and safety profile, with a reduced risk of serious adverse events [13]. Its ability to significantly reduce body weight while having a beneficial effect on cardiovascular risk factors makes it the optimal choice for the long-term management of obesity [17]. This novel pharmacological approach based on the GLP-1 mechanism is increasingly recognized by clinicians and patients alike as an effective and safe solution to the global obesity epidemic [18].

**Efficacy of semaglutide in clinical trials: results of meta-analyses**

The efficacy of semaglutide in reducing weight in obese patients has been widely recognized, as evidenced by the significant results observed in clinical trials [5]. Meta-analyses involving hundreds of participants have shown that semaglutide is associated with significantly greater weight loss than placebo [17]. The analysis revealed that participants who received semaglutide exhibited a greater propensity to achieve weight loss of ≥5%, ≥10%, ≥15%, and ≥20% in comparison to those who received a placebo. The placebo group exhibited minimal weight loss.

In comparison with the placebo, the use of semaglutide was associated with a significant reduction in long-term relative body weight. At the longest follow-up period, 33.4% of participants who were randomised to receive semaglutide achieved a weight loss of ≥20%, in contrast to 2.2% of those who received placebo [15].

It is notable that semaglutide demonstrated efficacy not only in terms of overall weight loss, but also in reducing body mass index (BMI) and waist circumference, which are important in assessing metabolic risk [9][18]. Furthermore, subgroup analysis indicated that semaglutide was effective across all demographic categories, including gender, age and initial body mass index, suggesting its potential use in a diverse range of obese patients [17]. In addition, the results of clinical trials are supported by strong evidence of improvements in obesity-related health indicators [19][17]. Significant reductions in blood pressure, LDL cholesterol and inflammatory markers such as C-reactive protein (CRP) were observed in patients taking semaglutide, suggesting the potential for cardioprotective benefits [13][20]. These changes are of supreme importance as obesity is a significant risk factor for the development of cardiovascular disease [21][22]. It is also worth mentioning the results regarding the long-term efficacy of the treatment. A number of studies have followed patients for up to two years to assess the durability of therapy effects These results suggest that semaglutide not only induces initial weight loss, but also facilitates the long-term maintenance of this loss, which is of greatest importance in preventing relapse to overweight [18][20][23]. This evidence supports the efficacy of semaglutide as a long-term obesity management strategy, offering patients a tangible opportunity to improve their health and quality of life [13].

**Safety of semaglutide: an overview of side effects**

While semaglutide has been shown to be highly effective in the treatment of obesity, it is equally important to understand its safety profile and the potential side effects that may occur during therapy. Clinical trials and meta-analyses suggest that semaglutide, like any drug, carries a certain risk of adverse effects. The most commonly reported reactions are gastrointestinal such as nausea, vomiting, diarrhea, and constipation [24]. Nausea, although usually mild to moderate, has the potential to affect patient comfort and may occasionally lead to discontinuation of therapy [17]. Notably, these symptoms are typically most pronounced at the start of treatment and tend to diminish as therapy progresses [15]. Another important aspect of the safety profile of semaglutide is its effect on blood glucose levels [25]. Although it is also used to treat type 2 diabetes, there is no increased risk of hypoglycemia in patients without diabetes, which is a significant advantage over other weight-loss drugs that can cause low blood glucose levels. The results of the study confirmed that the drug is safe for use in people who do not have a carbohydrate metabolism disorder, as blood glucose levels in patients treated with it remain within the normal range [17]. It is also worth noting that although semaglutide is associated with an increased risk of adverse events compared to placebo, the majority of these events are mild and transient in nature [17][15]. Such events are rare and rarely lead to significant complications [18]. With continued treatment, patients typically show improved tolerability over time [15]. However, it is imperative that patients are monitored for potential adverse effects, particularly during the first few weeks of therapy, so that an appropriate response, such as dose adjustment or temporary discontinuation, can be made.

In conclusion, although semaglutide has some side effects, its overall safety profile is favourable, particularly in view of its marked efficacy in reducing body weight and improving health parameters. With appropriate monitoring and management of adverse effects, it can be safely administered to the majority of obese patients and provide substantial health benefits [15][17][18].

**Potential cardiometabolic benefits associated with semaglutide therapy**

In addition to its efficacy in weight loss, semaglutide has been shown to have significant cardiometabolic benefits, which are of particular importance in obese patients, especially those at increased risk of cardiovascular disease. There is a strong association between obesity and the development of many metabolic disorders, including hypertension, dyslipidemia, and chronic inflammation [17]. These are significant risk factors for the development of cardiovascular disease and stroke [26]. Clinical studies have shown that treatment with semaglutide not only leads to weight loss, but also to significant improvements in health parameters that directly affect cardiometabolic risk. One of the most important effects of semaglutide is its ability to lower blood pressure. Statistical results showed that, compared with placebo, semaglutide significantly reduced SBP and showed a small reduction in DBP in obese patients [17]. In addition, semaglutide has been shown to have a beneficial effect on patients' lipid profile, lowering LDL cholesterol and triglycerides while increasing HDL cholesterol, which protects against heart disease [13][18][20]. Another important indicator of improved cardiometabolic well-being is a reduction in C-reactive protein (CRP) levels, which serve as an indicator of systemic inflammation. Elevated CRP levels are associated with an increased likelihood of developing cardiovascular disease [17]. Therefore, the reduction in CRP levels observed with semaglutide provides further evidence of the health benefits associated with this therapy [9][13][18]. As a result, this drug may help patients lose weight while reducing the likelihood of developing serious health complications associated with obesity, such as heart attack and stroke [17]. Furthermore, it is noteworthy that semaglutide has an effect on waist circumference, which is a robust indicator of metabolic risk [15]. The reduction in waist circumference observed in patients using semaglutide is indicative of a reduction in visceral fat, which is particularly dangerous for cardiovascular health. Taken together, these benefits make semaglutide not only a powerful tool in the fight against obesity, but also a key element in the prevention and treatment of cardiometabolic disorders. This makes it a medicine with a wide range of positive health effects.

**Future research directions and clinical perspectives for semaglutide**

Given the increasing prevalence of obesity and its associated health complications, future research into semaglutide and its potential applications represents a promising avenue to address this global health crisis. While existing studies have demonstrated the efficacy and safety of this drug in the treatment of obesity, there are numerous avenues for further investigation to fully realise its therapeutic potential. A promising direction for future research is to gain a deeper understanding of the molecular mechanisms underlying the impact of semaglutide, with a particular focus on its effects on energy metabolism and long-term weight regulation [15][18].

A deeper understanding of these mechanisms may facilitate the development of more effective therapies and the discovery of biomarkers to predict patient response to treatment. Another important area of research is to assess the long-term effects of semaglutide, both in terms of maintaining weight loss and its impact on metabolic and cardiovascular health over many years of therapy. There is a need for studies to determine how long semaglutide can be used safely and to determine the long-term benefits and potential risks of such therapy [24].

It is also important to consider the potential benefits of combining semaglutide with other therapies, including both pharmacological and non-pharmacological interventions such as lifestyle changes. The combination of drugs has the potential to increase the efficacy of obesity treatment, reduce the need for higher doses of individual drugs and minimise the risk of adverse effects. In addition, future research should focus on evaluating the use of semaglutide in different patient populations, including those with childhood overweight, older adults, those with metabolic disorders or other comorbidities. An expansion of the therapeutic indications may result in a significant increase in the availability of this medicine to a wider patient population that could potentially benefit from its use. Finally, the development of novel formulations of semaglutide, including oral versions or long-acting injections, may improve patient compliance and efficacy [17]. Research into these new forms of administration may facilitate novel approaches to the treatment of obesity and other metabolic disorders, improving accessibility and convenience for patients. In conclusion, although semaglutide already plays an important role in the treatment of obesity, future research and development of this therapy may further enhance its clinical value and offer new hope to patients struggling with obesity and its complications.

**Conclusion**

In summary, semaglutide represents a major breakthrough in the treatment of overweight, offering patients not only effective weight loss but also broad cardiometabolic benefits. Semaglutide's unique mechanism of action, based on modulation of satiety and regulation of energy metabolism, distinguishes it from other therapeutic options currently on the market. The efficacy of this treatment has been supported by a substantial body of clinical evidence demonstrating its ability to significantly reduce body weight and improve obesity-related health parameters, including blood pressure, lipid profile and inflammatory markers. However, more research is needed to fully understand the long-term effects of semaglutide and to determine the optimal use of the drug in different patient populations. In addition, the potential of this drug in combination with other therapies, both pharmacological and non-pharmacological, requires further analysis to ensure that its full therapeutic potential is realised.. In addition, the development of novel forms of semaglutide, including oral formulations, may improve its accessibility and convenience for patients. With its comprehensive benefits and robust safety profile, semaglutide has the potential to become the standard of care in the treatment of overweight, offering patients a real opportunity to improve their health and quality of life. As interest in the drug and its potential grows, it could play a key role in tackling the global epidemic of obesity and its associated health complications.

## Disclosure

### Author's contribution

Conceptualization, Wiktoria Bilska and Urszula Ciułek; methodology, Urszula Ciułek and Wiktoria Zduńczyk; software, Wiktoria Paduch-Jakubczyk; check, Michalina Dubińska, Anna Dobosz and Michalina Dubińska; formal analysis, Michalina Dubińska and Ada Żydek; investigation, Wiktoria Bilska; resources, Anna Dobosz, Ada Żydek and Wiktoria Zduńczyk; data curation, Anna Dobosz; writing - rough preparation, Wiktoria Paduch-Jakubczyk, Wiktoria Bilska and Anna Dobosz; writing - review and editing, Michalina Dubińska, Ada Żydek, Wiktoria Zduńczyk and Urszula Ciułek; visualization, Wiktoria Bilska; supervision, Wiktoria Paduch-Jakubczyk, Ada Żydek and Urszula Ciułek; project administration, Wiktoria Paduch-Jakubczyk and Wiktoria Zduńczyk; receiving funding, no specific funding.
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