Semaglutide in the Era of Blockbuster Pharmaceuticals: A Narrative Review of Clinical, Economic, and Policy Dimensions

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Abstract

The blockbuster drug model has become a central driver of growth in the pharmaceutical industry, generating substantial economic and healthcare impacts. Semaglutide, a glucagon-like peptide-1 (GLP-1) receptor agonist marketed under brand names such as Ozempic (subcutaneous, 0.25–1 mg for type 2 diabetes), Wegovy (subcutaneous, 2.4 mg for obesity), and Rybelsus (oral formulation), represents a contemporary example of a blockbuster pharmaceutical innovation demonstrating strong clinical performance alongside remarkable commercial success. This narrative review examines the clinical, economic, and policy dimensions of semaglutide's market trajectory. Since its approval, semaglutide has significantly improved glycemic control, promoted weight reduction, and reduced cardiometabolic risk, while becoming a major contributor to Novo Nordisk's financial growth and market leadership, most notably through the commercial launch of Ozempic, which served as a primary catalyst for the company's rise to become one of the world's most valuable pharmaceutical corporations. Its rapid global adoption has expanded the therapeutic landscape for metabolic diseases and stimulated further pharmaceutical innovation. However, increasing demand, off-label utilization, supply shortages, access disparities, reimbursement challenges, and rising healthcare costs have introduced important regulatory, ethical, and sustainability considerations. Semaglutide illustrates the evolving relationship between biomedical innovation, pharmaceutical economics, and healthcare policy, highlighting both the benefits and challenges of blockbuster drug success in modern healthcare systems.

Keywords: semaglutide; Ozempic; blockbuster drugs; economic impact

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Introduction

The term *blockbuster* originated in the film industry and was later adopted in the pharmaceutical domain to describe highly profitable drugs. Their market success, typically reflected in annual revenues exceeding one billion US dollars, is driven by broad therapeutic applicability, demonstrated clinical effectiveness, and the ability to address unmet medical needs. Since the late 1980s, blockbuster drugs have become a cornerstone of pharmaceutical business models, serving as key drivers of economic stability, market growth, and innovation. Backed by substantial investments in research and development, as well as extensive commercialization strategies, these therapies represent both scientific progress and economic value creation. Their global reach enables treatment across diverse populations, contributing to improved health outcomes and broader public health benefits. Concurrently, blockbuster drugs remain fundamental to the financial sustainability and long-term innovative performance of the pharmaceutical industry (1–3). Semaglutide (Ozempic), a next-generation antihyperglycemic therapy for the contemporary management of type 2 diabetes, exemplifies the modern blockbuster drug model and represents a highly impactful product in the global pharmaceutical marketplace. Developed by Novo Nordisk, semaglutide emerged from research and development efforts that positioned it for broad clinical applicability and sustained market relevance. Its financial performance has significantly enhanced the company's capital strength, expanded its global footprint, and reinforced its long-term competitive advantage. The case of semaglutide highlights how pharmaceutical innovation can simultaneously address pressing global health needs and generate substantial economic value within an increasingly competitive industry landscape (4,5).

The Clinical and Commercial Success of Semaglutide

Semaglutide (Ozempic), a glucagon-like peptide-1 (GLP-1) receptor agonist, represents a major therapeutic advancement in the management of type 2 diabetes. Its pharmacological action encompasses enhanced glucose-dependent insulin se-cretion, suppression of glucagon release, delayed gastric emptying, and reduced appetite, collectively resulting in improved glycemic regulation and weight reduction. Despite the availability of multiple effective antihyperglycemic therapies, an unmet need persisted for a treatment capable of achieving superior glycemic control while simultaneously providing cardiovascular and renal protection. Such benefits include preservation of renal function, reduction in blood pressure, and prevention of cardiovascular events, which remain common complications among patients with type 2 diabetes. Accordingly, the development of a more efficacious therapeutic approach was warranted for patients with inadequate disease control despite diet, physical activity, oral antihyperglycemic medications, or insulin therapy (6). Novo Nordisk, the developer of semaglutide, has established itself as a global leader in the management of diabetes and obesity. The company's research framework emphasizes not only therapeutic intervention but also prevention and sustained improvement of patient outcomes. Through continued investment in research and development, Novo Nordisk has combined molecular innovation with comprehensive disease management strate-gies.

The first glucagon-like peptide-1 (GLP-1) receptor agonist, exenatide, was approved by the U.S. Food and Drug Administration (FDA) in 2005, marking the beginning of a new therapeutic class for the management of type 2 diabetes. In the years that followed, additional GLP-1 receptor agonists, such as liraglutide and dulaglutide, were introduced, progressively expanding treatment options and improving glycemic management. Despite these advances, limitations related to dosing frequency, adherence, and the magnitude of metabolic benefits remained. Semaglutide represents a next-generation

agent within this class, characterized by once-weekly subcutaneous administration (0.25 mg, 0.5 mg, and 1 mg; Ozempic), improved pharmacokinetic stability due to albumin binding and structural modifications, and more pronounced effects on glycemic control and body weight.

An oral formulation of semaglutide (Rybelsus, 7 mg and 14 mg) was subsequently approved, further broadening its clinical applicability. These advantages significantly contributed to the rapid expansion in the clinical use of GLP-1 receptor agonists following the introduction of semaglutide (7).

The U.S. Food and Drug Administration approved semaglutide (Ozempic, 0.25–1 mg subcutaneous) for the treatment of type 2 diabetes in December 2017. Randomized clinical trials consistently confirmed its effectiveness in improving glycemic control, promoting weight reduction, improving cardiometabolic risk factors, and supporting renal function (8–14). During clinical development, researchers observed significant weight loss among treated patients, attributed to both central and peripheral mechanisms, including reduced caloric intake, decreased appetite between meals, enhanced satiety, and delayed gastric emptying, effects mediated through GLP-1 receptor activation in the hypothalamus and gastrointestinal tract. These findings subsequently supported the development and approval of a higher-dose subcutaneous formulation (semaglutide 2.4 mg; Wegovy) specifically indicated for chronic weight management in adults with obesity or overweight with at least one weight-related comorbidity.

These effects are primarily attributed to GLP-1–mediated signaling that influences central appetite regulation pathways. Clinical trials of higher-dose semaglutide (2.4 mg; Wegovy) have demonstrated average body weight reductions of approximately 15–16% from baseline, with some participants achieving reductions exceeding 20% (15,16). It should be noted that such pronounced weight loss data largely derive from trials conducted at the obesity-indicated dose, rather than from the diabetes-indicated formulation (Ozempic, 0.25–1 mg). Although semaglutide was originally developed and approved for the management of type 2 diabetes, its notable weight-reducing effects led to a substantial increase in off-label use among individuals without diabetes, raising important considerations regarding equitable access, drug supply, and appropriate prescribing practices.

Semaglutide is marketed by Novo Nordisk under distinct brand names, each corresponding to a specific formulation, indication, and dosing regimen, a distinction of considerable clinical and regulatory importance. Ozempic is a once-weekly subcutaneous formulation of semaglutide approved for the management of type 2 diabetes, administered at doses of 0.25 mg, 0.5 mg, and 1 mg. Rybelsus is the first oral formulation of semaglutide, approved for type 2 diabetes at doses of 7 mg and 14 mg. Wegovy is a higher-dose once-weekly subcutaneous formulation (2.4 mg) approved for chronic weight management in adults with obesity or overweight with at least one weight-related comorbidity. The approval of Wegovy further expanded the therapeutic role of semaglutide and contributed to the growth of pharmacological treatment options for obesity. Clinicians have increasingly incorporated semaglutide into individualized treatment strategies, particularly in patients presenting with the concurrent burden of type 2 diabetes and obesity — a clinical phenotype increasingly referred to as "diabesity" (16).

Diabesity represents a major global health concern, and even modest weight reduction of 5% has been associated with meaningful metabolic and cardiovascular benefits (16). Semaglutide's ability to induce clinically significant weight loss, particularly at the 2.4 mg dose (Wegovy), has broadened its therapeutic potential beyond type 2 diabetes, positioning it as a key agent in modern weight management strategies. The growing clinical success of semaglutide has also stimulated research into additional therapeutic indications, including metabolic dysfunction-associated steatohepatitis (MASH), chronic kidney disease, cardiovascular risk reduction

in non-diabetic populations, and addiction-related behaviours, reflecting the broad physiological reach of GLP-1 receptor activation.

Metabolic dysfunction-associated steatotic liver disease (MASLD) is highly prevalent in patients with type 2 diabetes and is characterized by metabolic dysfunction and progressive liver injury. In a phase 2 randomized controlled trial, semaglutide demonstrated a significantly higher rate of metabolic-associated steatohepatitis (MASH) resolution without worsening of fibrosis compared with placebo (17).

Clinical trials have evaluated the effects of semaglutide on major adverse cardiovascular events, demonstrating significant reductions in cardiovascular risk (18–20). Cardioprotective effects have been attributed to improvements in glycemia, blood pressure, body weight, and direct anti-inflammatory and endothelial-protective mechanisms. Semaglutide has additionally demonstrated improvements in renal outcomes, including reduced albuminuria and slower progression of chronic kidney disease (18–20).

Impact on Corporate Portfolio and Market Position

Annual reports from Novo Nordisk document the rapid revenue growth attributable to semaglutide (Ozempic). Sales increased from USD 284 million in 2018 to USD 3.24 billion in 2020, reflecting accelerating global adoption following initial market authorization. In the first nine months of 2023, semaglutide (Ozempic) generated approximately USD 4.8 billion in the third quarter alone, representing approximately 52% of Novo Nordisk's total revenue of USD 23.6 billion for that period. These figures illustrate the substantial commercial impact of semaglutide and its central role in Novo Nordisk's financial performance and capacity for continued research investments (21).

The commercial success of semaglutide has profoundly transformed Novo Nordisk's position in the global pharmaceutical landscape. At its peak market capitalization in 2023, Novo Nordisk briefly became Europe's most valuable publicly traded company. From a specialized diabetes-focused pharmaceutical company, Novo Nordisk has evolved into a global corporation employing approximately 60,000 people across more than 80 countries. The rising global prevalence of obesity and type 2 diabetes has further increased demand for effective metabolic therapies, consolidating the company's position as a leading player in the global pharmaceutical market (22).

In 2023, Novo Nordisk's stock price increased by 54%, with the company holding 33.3% of the global diabetes value market and 54.3% of the GLP-1 segment, according to data from the independent data provider IQVIA. Semaglutide (Ozempic) represented a dominant share of diabetes product revenue. Analysts project continued market expansion (23).

The commercial success of semaglutide has stimulated mergers, acquisitions, and strategic partnerships within Novo Nordisk's broader corporate strategy. Among these, the acquisition of Dicerna Pharmaceuticals in 2021 expanded the company's research capacity in RNA-based therapies targeting metabolic and liver diseases (24). With patent protection for semaglutide expected until approximately 2031, the molecule is projected to remain a key driver of Novo Nordisk's commercial performance in the near term. However, patent expiry will likely stimulate the entry of biosimilar and generic competitors, with potential implications for drug pricing, market share, and patient access (25).

Adverse and Regulatory Considerations

Despite its clinical efficacy, semaglutide is associated with a recognized adverse effect profile that warrants careful consideration. Gastrointestinal adverse effects, including nausea, vomiting, diarrhea, and constipation, are among the most frequently reported, particularly during dose escalation. More serious complications, including gastroparesis and intestinal obstruction, have been reported in post-marketing surveillance. Additionally, the prescribing information carries a boxed warning regarding the risk of thyroid C-cell

tumors observed in animal studies, and caution is advised in patients with a history of pancreatitis (26).

Another important consideration relates to the long-term management of therapy. Although semaglutide has demonstrated substantial benefits in weight reduction, the optimal duration of treatment and long-term maintenance strategies remain under investigation. Evidence suggests that individuals who discontinue treatment often regain a significant proportion of the lost weight, indicating that sustained therapy or additional lifestyle interventions may be necessary to maintain therapeutic benefits (27).

The growing demand for semaglutide, particularly for weight management, has significant implications for health policy across Europe. Increased off-label use has contributed to supply shortages, prompting regulatory measures in several countries aimed at prioritizing access for patients with type 2 diabetes.

Considerable variation across healthcare systems regarding the reimbursement of semaglutide for obesity indications has further shaped equitable access. These developments highlight broader challenges related to drug availability and the sustainability of healthcare expenditure in the context of rapidly expanding therapeutic demand (28,29).

Conclusion

Semaglutide has demonstrated significant clinical benefits across multiple therapeutic domains, including glycemic control, weight reduction, blood pressure management, cardiovascular risk reduction, and renal function preservation. This narrative review highlights how semaglutide exemplifies the modern blockbuster drug model, simultaneously addressing major unmet clinical needs and generating substantial commercial success. Simultaneously, rising healthcare expenditures, off-label utilization, supply shortages, access disparities, and reimbursement challenges raise important economic and policy considerations that extend beyond clinical efficacy. The success of semaglutide has stimulated broader pharmaceutical innovation and regulatory adaptation, while also exposing systemic tensions between drug pricing, equitable access, and the long-term sustainability of the healthcare system. Pharmaceutical companies, payers, and regulators must collectively address these challenges to ensure that the benefits of pharmacological innovation are accessible in diverse healthcare settings. Overall, semaglutide represents a compelling contemporary example of how biomedical innovation can reshape pharmaceutical economics, healthcare policy, and global therapeutic markets, underscoring the need for robust evidence-based frameworks to guide its continued clinical and commercial development.

Declarations

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