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Client Alert: Wegovy – A Wonder Weight Loss Drug (If you can get it.)

In June 2021, Danish drug maker Novo Nordisk received FDA approval for Wegovy (*Semaglutide*), a weight-management drug administered via weekly injection. When used in combination with improved eating and exercise, Wegovy can deliver remarkable results for adults diagnosed as being unhealthily overweight or obese. Shortly after its release, just as demand for the drug began seeing rapid growth, Novo Nordisk started experiencing

manufacturing issues. To date (15 months after its release), demand continues to outpace supply considerably.

Many patients, unable to acquire Wegovy at a local pharmacy or because they do not qualify for coverage under their health plan, have turned to alternative sources promising to deliver lower cost *Semaglutide* or *Semaglutide* -like substitutes to consumers. Telehealth startups, compounding pharmacies, and physician entities offering wellness care have popped up, attracting consumers who want to access the 'wonder weight-loss drug.' For the wellness and cosmetic healthcare industry, Wegovy could be a real boon.

At the same time, pharmacy stakeholders are raising concerns that ongoing *Semaglutide* shortages are leading to a marketplace for "bootleg" reformulations that are technically illegal. The popularity of the gut hormone Gluconlike Peptide-1 or "GLP-1" pre-dates Wegovy, as alternative medical practices have long embraced the GLP-1 (along with other peptides). This naturally occurring hormone does two appealing things: (1) It stimulates production of insulin thus reducing blood-sugar levels for individuals with diabetes, and (2) it slows down digestion by signaling the brain when a person's stomach is full.

The legal problem with the so-called "generic" semaglutide is that, for years, as a naturally occurring substance, GLP-1 lacked any patentable intellectual property that would motivate a drug company to incur the expenses involved in seeking FDA approval. As a consequence, like most peptides, GLP-1 remained an unapproved drug for purposes of the Food, Drug, and Cosmetic Act, making it illegal for doctors to utilize. At the same time, the efficacy of GLP-1, coupled with a lack of any demonstrated FDA effort in cracking down on its use, meant that it continued to be popular in anti-aging and regenerative medical practices, with positive results. GLP-1 presented a conundrum: an effective weight loss drug that was technically illegal to prescribe under U.S. drug laws.

For Novo Nordisk, the success in identifying patentable elements in GLP-1 to justify the approval costs associated with Wegovy was the capstone of a quarter-century effort to produce an effective and marketable weight management medication based on GLP-1. While Novo Nordisk is a major participant in the diabetic drug and insulin market (which includes 33 million people with type-2 diabetes), diabetes medicine itself is a mature market saturated with brand-name drugs and generic alternatives. By comparison, the outlook for a safe and effective prescription weight-loss drug is immense. In 2020, the CDC considered 41% of Americans—over 100 million individuals—to be clinically overweight. Considering the numerous health risks that accompany obesity, any medication that can meaningfully reduce these statistics would be enthusiastically embraced by the healthcare marketplace.

Exploiting GLP-1's hunger-suppressing capabilities presented certain challenges for Novo Nordisk, including the ready availability of GLP-1 on the international market. Numerous companies, including ThermoFischer and Sigma Aldrich (a subsidiary of Merck), market a variety of GLP-1 based products for research or clinical use. As noted above, the FDA is generally opposed to offering patent protections to synthetically made reproductions of hormones and biologics produced naturally in the human body. In addition, the widely available GLP-1 is reputed to have short-lived benefits in suppressing hunger, typically lasting 30 minutes to an hour. For Novo Nordisk, the challenge was creating a GLP-1 analog *sufficiently* different from the original to give it IP protection, and *sufficiently* altered to suppress hunger on a daily or weekly duration.

In 2010, Novo Nordisk launched Victoza (*Liraglutide*), a *daily* GLP-1 based injection that helps regulate glucose levels for type 2 diabetes. The medication quickly became a billion-dollar earner for the multinational. Then, using the same formulary, Novo launched Saxenda in 2014, as a weight-management drug. The drug rose to a top spot for weight management despite clinical trials showing rather modest results. In one study, 59% of participants lost 5% or more of their body weight when *Liraglutide* was used in conjunction with Metformin and "lifestyle

intervention"—but the additions of another drug and lifestyle changes raised questions of just how much *Liraglutide* was contributing. But Novo kept at it, launching an improved GLP-1 *weekly* injectable for diabetes in 2017, under the brand name Ozempic (*Semaglutide*). Again, this was followed four years later by its approval as a weight loss drug under the Wegovy brand name. This time, the clinical trials were much better. In one study, average participants lost 15% of their body weight over a 68-week period.

Social Media and Off-Label Prescribing

When Wegovy shortages first emerged, many physicians shifted to off-label Ozempic prescriptions for their patients who needed or wanted to lose weight but could not access Wegovy. This trend intensified under the influence of TikTok social media campaigns promoting *Semaglutide*, eventually leading to Ozempic shortages as well. In Australia, alarming concerns over insufficient supply for diabetics persuaded government and multiple medical associations to request that doctors prioritize type 2 diabetes patients. Off-label prescribing caused similar issues in the United States, with the FDA adding Ozempic to the drug shortages list in late August.

Is there "Bootleg" *Semaglutide* on the Market?

Despite ongoing shortages and limited availability across the pharmacy sector, there remains hundreds of weight loss-oriented drug providers and body-wellness clinics that continue to advertise Wegovy, Ozempic, or *Semaglutide* online. It appears that many of these providers are offering other versions of GLP-1 than the Novo Nordisk product. This raises issues related to the FDA status of the product, potential infringement of Novo Nordisk's patent, as well as sourcing and supply-chain questions. There is no approved "generic" form the FDA-approved product in this case, leaving the existing GLP-1 supply as an unapproved substance.

One major source of GLP-1/*semaglutide* has been compounding pharmacies. Federal law recognizes two types of compounding pharmacies, "503A" pharmacies which modify and fill prescriptions specifically tailored to a single patient, and "503B" outsourcing facilities, which are essentially outsourcing manufacturers that will compound bulk drug substances for healthcare facilities to use more broadly. As 503A compounding pharmacies are state-regulated, oversight can vary widely. The vast majority of state pharmacy regulators are not attuned to the questionable FDA status of particular products. Federal law prohibits 503B facilities prohibited from manufacturing drugs that are "identical or nearly identical to an approved drug unless the approved drug appears on the drug shortage list." With both Wegovy and Ozempic on the FDA's shortage list, registered 503B manufacturers could be forgiven for mistakenly believing they are authorized to produce and supply *Semaglutide* to healthcare facilities and physician offices. The question is whether the FDA will intervene or whether Novo Nordisk will elect to pursue potential patent infringement claims. In the past, the FDA has been reluctant to invest resources unless and until media attention is drawn to incidents of patient harm, something that has not happened with GLP-1. According to Novo Nordisk, *Semaglutide* shortages will likely to persist into 2023. For compound pharmacies, physicians, and patients electing to utilize the unapproved versions of the drug, caution is warranted.

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