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Compounded GLP-1 Drugs: is the Party Over? These Are the Legal and Regulatory Issues for Game Changing Weight Loss Products and the Companies Selling Them

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Glucagon-like peptide-1, or "**GLP-1**" drugs, such as Ozempic® and Mounjaro®, have exploded in popularity in the United States for weight management and the treatment of obesity. However, GLP-1 drugs were not originally intended for that purpose, and their manufacturers have struggled to satisfy consumer demand. This supply/demand mismatch has resulted in well documented shortages which have, as a matter of law, authorized compounding pharmacies to make copycats. However, as supply inches towards demand, complex legal questions arise driven by FDA regulations and the monopoly protections afforded to patentholders.

This article explores what's next for these generationally popular weight loss drugs. Stay tuned to the end for important takeaways and action items.

A. Approved GLP-1 drugs and market exclusivity.

GLP-1 is a hormone found in a class of injectable drug products ("GLP-1 drugs") which lower serum glucose levels and thereby manage metabolism for patients with diabetes and obesity disorders. Examples of GLP-1 drugs include the following:

Chemical Name	Brand Name
Dulaglutide	Trulicity®

Exenatide	Byetta®
Liraglutide	Victoza® and Saxenda®
Lixisenatide	Adlyxin®
Semaglutide	Ozempic® and Wegovy®
Tirzepatide (GLP-1 receptor agonist)	Mounjaro® and Zepbound®

FDA's approvals of GLP-1 drugs for weight loss is a fairly recent phenomenon. As an example, FDA approved the first GLP-1 drug (Byetta®) in 2005 for patients with type 2 diabetes, and many products followed suit with similar indications. In 2014, Novo Nordisk's liraglutide (Saxenda®), a daily injection, was the first GLP-1 to receive FDA approval for "chronic weight management, and in 2022 FDA approved semuglutide Wegovy® as a weekly injection with a similar indication. Of course, in tandem with their efforts to obtain FDA approvals, the manufacturers of these products sought and obtained patent protection, which effectively prohibited other companies from making copycats involving the patented or drug substances (exenatide, semaglutide, and so on).

In most instances, the combination of FDA approval and patent protection affords the manufacturer a legally protected monopoly over the drug substance in the United States, sometimes for 12 years or longer until the patent expires and generics can enter the market. In addition to the lawsuits patentholders can file to protect their monopolies, FDA plays a key gatekeeping function by reviewing patent information as part of drug approval applications, taking care to not approve the same patent-protected drug substance twice. *See* 21 U.S.C. § 355(b)(1)(viii).

This monopoly power is commonly seen as a well-deserved reward to the manufacturer for its investment in research and development and discovery of new drugs to benefit the public health. As one court has explained:

The system of developing new drugs in this country exemplifies the maxims "no risk, no reward" and "more risk, more reward." Developing new drugs is a risky, lengthy,

and costly endeavor, but it also can be highly lucrative. Only one in every 5,000 medicines tested for the potential to treat illness is eventually approved for patient use, and studies estimate that developing a new drug takes 10 to 15 years and costs more than $1.3B. **No rational actor would take that kind of a risk over that period of time without the prospect of a big reward.**. The reward, if any, comes when the drug is approved and patented, giving the pioneer or "brand name" company that developed it a monopoly over the sale of the new drug for the life of the patent. The pioneer company can then exploit the patent monopoly by charging higher prices than it could if competitors were allowed to sell bioequivalent or "generic" versions of the drug. In that manner, the pioneer company is usually able to recoup its investment and gain a profit, sometimes a super-sized one.

FTC v. Watson Pharma., 677 F.3d 1298, 1300 (11 th Cir. 2021) (emphasis added) (overruled on other grounds as stated in *FTC v. Actavis*, 570 U.S. 136 (2013).

In spite of this awesome monopoly protection for approved, patented drugs, important exceptions exist, which is how we arrived where we are today with compounded copies of GLP- 1 drugs proliferating the market.

B. Compounding Pharmacies and GLP-1 drugs.

Traditionally, compound pharmacies played a local, niche role in the U.S. drug supply chain, specifically by mixing drug ingredients tailored to the needs of individual patients. *See e.g. Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 360–61 (2002). "Compounding is typically used to prepare medications that are not commercially available, such as medication for a patient who is allergic to an ingredient in a mass-produced product." *Id.*, at 361. Given that local, niche role, the regulators of first resort were state pharmacy boards, rather than FDA.

Inevitably, however, compound pharmacies outgrew their traditional role, and bad things happened resulting in federal legislation. Specifically, in 2012, the New England Compounding Center made and distributed three lots of epidural steroid injections which were tainted with fungal meningitis and distributed in interstate commerce leading to 48 patient deaths and more than 700 cases of persistent fungal

infections.

After the ensuing congressional investigation, in 2013 Congress passed the Drug Quality and Security Act (DQSA), which created a new category of compounders called "outsourcing facilities." *See* 21 USC § 353b. Unlike the "traditional" compound pharmacies making individualized products for individual patients, § 353b allows outsourcing facilities to manufacture large amounts of drugs without individually identifiable patients and prescriptions, subject to i) good manufacturing practice requirements, and ii) routine FDA inspections. Traditional compounders, *i.e.* those which make compounded drugs for individual patients, are subject to regulation by 21 USC § 353a.

To be clear, in the vast majority of circumstances, §§ 353a and 353b make clear that compound pharmacies and outsourcing facilities cannot make copycats of approved, commercially available drugs. *See* § 353a(b)(1)(D) (prohibiting compounders from compounding "regularly or in inordinate amounts…any drug products that are essentially copies of a commercially available drug product."); § 353b(a)(5) (prohibiting the compounding of a drug which is "essentially a copy of one or more approved drugs.")

However, even if a particular drug is approved and a manufacturer has a legally authorized monopoly over it, § 353b includes an important carveout allowing for the compounding of "copies" if the drug is on a "shortage list" published and maintained by FDA pursuant to 21 USC § 356e. Federal law defines "drug shortage" as "a period of time when the demand or projected demand for the drug in the United States exceeds the supply," 21 USC § 356c(h)(2), and FDA considers a shortage "resolved" when "all the manufacturers are able to meet total national historical demand."

This is the statutory authority upon which compounded copies of FDA approved GLP-1 drugs have proliferated in the United States – creating greater access at a lower cost for patients, albeit with a greater safety risk than the approved, brand named versions. Indeed, as of this moment, all of the GLP-1 drugs on the list above, with the exception of Tirzepatide (Mounjaro®) (discussed below), remain on FDA's drug shortage list, so outsourcing facilities can continue making copies of them.

C. Tirzepatide (Mounjaro® and Zepbound®) and FDA's Drug Shortage List

Tirzepatide, known by its brand names Mounjaro® (for diabetes) and Zepbound® (for weight loss), is a GLP-1 drug over which Eli Lilly & Co. ("Lilly") has a legal monopoly. In December 2022, as demand for all GLP-1 drugs skyrocketed with the news that they could be safe and effective for obesity and weight management, FDA included tirzepatide on its shortage list, which opened the floodgates for compounded copies.

But as the FDA giveth, the FDA taketh away, and companies in the compounded tirzepatide business are now confronting the reality of Lilly having pumped billions of dollars into its manufacturing capabilities and an urgent shareholder demand to recoup the profit. To their credit, public companies distributing compounded GLP-1 drugs have acknowledged this risk. *See, e.g.* Hims & Hers Health, Inc., Form 10-Q, June 30, 2024 ("Additionally, certain aspects of the GLP-1 compounding to which we offer access is based on current shortages of branded GLP-1s, and we cannot predict when such shortages will be resolved. While FDA does not limit compounding to drug shortages and we believe there are paths to continue offering access to certain compounded GLP-1s after the shortage ends, we cannot guarantee that we will be able to continue offering these products in the same manner, to the same extent, or at all, due to a variety of factors outside our control, including supply chain, intellectual property, regulatory and resource allocation matters.")

On October 2, 2024, this risk materialized when FDA announced on its website that Lilly had resolved the tirzepatide shortage, meaning that companies making and distributing compounded copies needed to stop in their tracks, regardless of ongoing patient care. However, on October 7, 2024, the Outsourcing Facilities Association ("**OFA**") filed suit against FDA in federal court in Fort Worth, alleging that FDA's decision to remove tirzepatide from the shortage list violated the Administrative Procedure Act (APA) because, *inter alia*, FDA failed to provide notice and seek comments from affected stakeholders. In response to the OFA lawsuit, FDA announced on October 11 that it was re-evaluating its position and

promised to publish a final decision by November 21. In the meantime, FDA also committed that it would not take action against compounders for making copies of tirzepatide.

D. What happens to companies compounding or distributing "copies" of GLP-1 drugs after shortages are resolved?

To the extent a particular GLP-1 drug (for instance, tirzepatide or semaglutide) is removed from FDA's shortage list, and to the extent compounders and telehealth companies continue making and selling copies, they are subject to enforcement by FDA and, courts have held, civil liability to the drug company who owns the patent.

Primarily, when a compounding pharmacy creates a copy of an approved drug which is not subject to a shortage as determined by FDA, the compounder is no longer immune from the federal misbranding and unapproved new drug statutes, both of which could result in FDA enforcement and serious regulatory consequences. However, given the resources available to major drug companies (e.g. Lilly), the more likely course of action is the drug companies taking the enforcement lead, as Lilly just did during the brief period after OFA filed its suit and before FDA pressed pause on its decision that the terzepatide shortage had been resolved.

In most cases, private litigants are barred from weaponizing another party's FDA compliance status in litigation because, under federal law, only the FDA can. *See* 21 U.S.C. § 337(a) ("…all such proceedings for the enforcement, or to restrain violations, of this chapter shall be by and in the name of the United States.") *See e.g. Buckman Co. v. Plaintiffs' Legal Committee*, 531 U.S. 341, 349, n.4 (2001) ("The FDCA leaves no doubt that it is the Federal Government rather than private litigants who are authorized to file suit for noncompliance with the medical device provisions…").

In spite of § 337, in two recent cases courts have held that private litigants ***can*** enforce the shortage list in court – specifically by bringing Lanham Act suits for unfair competition and false advertising. First, in *Azurity Pharmaceuticals Inc. v. Edge Pharma, LLC*, 45 F.4 th 479 (1 st Cir. 2022), the First Circuit reversed the

District of Massachusetts which held otherwise because "the adjudication of this claim simply requires a court to ascertain whether a particular drug appears" on the shortage list. *Id.*, at 501. In other words, for the First Circuit, why leave it to FDA if the violation is readily apparent? In *Pacira Biosciences Inc. v. Quva Pharma Inc.*, No. 23-cv- 4147, 2024 WL 4329142 (S.D. Tex. Aug. 26, 2024), the court reached the same result, specifying that "a claim that merely requires a court to cross-reference a list is not precluded," but "claims that require a court to interpret, apply, or enforce the FDCA remain precluded."

Such is the importance of FDA's shortage list and OFA's lawsuit against FDA. If FDA does not place tirzepatide back on its shortage list, compounded copies will be fair game in court for Lilly and Novo, and companies like Hims and others selling them will need to need to prepare their litigation strategies and/or quickly find alternative products. Of course, different courts today may interpret the law differently given the widespread use of compounded tirzepatide and semaglutide and the added consumer cost prohibition will inevitably create. Meanwhile, if OFA can convince the court to enjoin FDA and require that tirzepatide return to the shortage list pending rulemaking procedures, there could be some breathing room, but that case is an uphill battle.

E. Next Up: Novo Nordisk argues that semaglutide is too difficult to compound.

In addition to the purported resolution of the GLP-1 shortages, Novo Nordisk has challenged the regulatory status of compounded GLP-1 drugs by petitioning FDA to prohibit compounding pharmacies from making copies of semaglutide because it is too complex to do so with any guarantee of safety or effectiveness. This argument is premised on separate provisions of 21 USC §§ 353a and 353b which authorize FDA to create and maintain a list of drugs that present "demonstrable difficulties" for compounding. Novo's argument is a shot across the bow for ***all*** compounded GLP-1 products, and the industry should expect other manufacturers to follow suit with a wave of similar challenges.

Novo's path forward on this issue, however, is a slog – because unlike the shortage

list, § 353b requires that FDA implement the "demonstrably difficult" list "by regulation." Moreover, the statute requires that FDA convene an "advisory committee" on compounding which "shall include representatives from the National Association of Boards of Pharmacy, the United States Pharmacopeia, pharmacists with current experience and expertise in compounding, physicians with background and knowledge in compounding, and patient and public health advocacy organizations." *See* 21 USC § 353b(c). Thus, even assuming Novo's argument has merit, FDA's proposed rule implementing the list is still not final, and no GLP-1 drug was nominated as "demonstrably difficult" in the first draft. Given Novo's purported resolution of the semaglutide shortage, its argument that semaglutide is too complex for compounding will likely take a back seat.

F. Takeaways and Action Items

Over the past two years, compounded copies of GLP-1 drugs have proliferated based on unique market conditions and corresponding accommodations under federal law. However, as patentholders ramp up their manufacturing capabilities, the accommodations fade, and the risk of FDA enforcement and civil litigation reappear.

Companies, including telehealth firms and compounding pharmacies, should expect and prepare for the following:

- Lilly and Novo have convinced FDA that the shortage of their respective GLP-1 drugs has resolved. If FDA does not return tirzepatide and semaglutide to its shortage list, companies compounding and selling them will need to prepare for litigation and/or find alternative products.

- Novo has petitioned FDA to place semaglutide on a list of drugs which are too difficult to compound – but FDA will need to submit that request to a notice and comment rulemaking process. Companies compounding and selling copies should be prepared to participate in the rulemaking and have their voices heard, keeping in mind that manufacturers of other GLP-1 drugs can bring similar petitions of their own at any time.

- Petitions to either remove GLP-1 drugs from FDA's shortage list or place them

on FDA's "demonstrably difficult" list will continue – so all companies in the space should stay vigilant.

- Companies adulterating or misbranding compounded GLP-1 drugs remain subject to FDA enforcement and litigation against patentholders regardless of FDA's shortage list.

Ultimately, as already proved by the events of October 2024, major changes may continue to occur with little or no notice – and stakeholders should expect the only constant to be change.

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