Alliance for Pharmacy Compounding
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Compounded GLP-1 Drugs and Patient Adverse Events

Background

Recent comments by Novo Nordisk's CEO Lars Jorgensen about serious adverse events he says are associated with compounded semaglutide have been widely reported. Jorgensen cites data drawn from FDA's Adverse Event Reporting System (FAERS) as the source of that information. What was omitted in his comments and largely in the reporting of them is necessary context.

Here, we share information about FAERS and patient adverse events reported via that system – as well as the challenges of relying on information reported to FAERS.

What is FAERS and How Does It Work?

- As the name implies, the FDA Adverse Event Reporting System (FAERS) is a reporting tool maintained by the agency for reporting of human patient adverse events associated with commercially available and FDA-approved drugs as well as compounded drugs. (There is no formal adverse events reporting system for animal drugs.)
- Reporting to FAERS is largely voluntary for patients, physicians (and other prescribers), and pharmacists. However, federal law does require reporting by makers of FDA-approved drugs and by 503B outsourcing facilities (503Bs are entities registered with FDA that produce drugs and distribute them to hospitals, clinics and pharmacies without a patient-specific prescription).
- The reporting of an adverse event in FAERS is not an indication that the drug in question caused the adverse event or even that the adverse event has been investigated. Indeed, FAERS makes these disclaimers on its home page:
    - **Existence of a report does not establish causation:** For any given report, there is no certainty that a suspected drug caused the event. While consumers and healthcare professionals are encouraged to report adverse events, the event may have been related to the underlying disease being treated, or caused by some other drug being taken concurrently, or occurred for other reasons. The information in these reports reflects only the reporter's observations and opinions.
    - **Duplicate and incomplete reports are in the system:** There are many instances of duplicative reports and some reports do not contain all the necessary information.
    - **Information in reports has not been verified:** Submission of a report does not mean that the information included in it has been medically confirmed nor is it an admission from the reporter that the drug caused or contributed to the event.

- Not all reported adverse events are considered serious, and indeed, a quick scan of reports in the system shows that many reported adverse events associated with both FDA-approved and compounded drugs are not serious and/or are known side effects of the drug in question. FDA defines a serious adverse event as one that:
  1. Results in death.
  2. Is life-threatening.
  3. Requires inpatient hospitalization or causes prolongation of existing hospitalization.
  4. Results in persistent or significant disability/incapacity.
  5. May have caused a congenital anomaly/birth defect.
  6. Requires intervention to prevent permanent impairment or damage.

- FAERS indicates that FDA *does* conduct an expedited investigation of reported serious adverse events associated with commercially available or compounded drugs when those serious adverse events are *not* known potential side effects of the drug.

Parsing the Data

Any serious adverse event is concerning, whether it is related to a compounded or a commercially available drug, and merits prompt and thorough investigation.

Mr. Jorgensen said in his comments to CNN that the source of the numbers he quoted – 10 patient deaths and 100 hospitalizations – was FDA's Adverse Event Reporting System (FAERS). And indeed, the site allows for flagging compounded adverse events versus those for manufactured drugs. For compounded semaglutide (the active pharmaceutical ingredient (API) in Novo Nordisk's GLP1 drugs), that flagging indicates 496 adverse events reports, 378 identified as serious, and of those, 11 indicate a patient died while taking compounded semaglutide. These reported deaths are absolutely heartbreaking regardless of the cause. But FAERS does not indicate that the compounded drug caused the death, only that the patient was reported to have been taking compounded semaglutide. That's why thorough investigation of reports of serious adverse events is essential. Often patients may be taking other drugs or have certain conditions and co-morbidities that may have contributed to or have been the cause of their death.

What Mr. Jorgensen did not mention, but which is also documented in FAERS is the following:

- As of November 11, 2024, FAERS reports a total 16,662 serious events and 505 patient deaths associated with semaglutide. All but 51 of the reports of patient deaths are accompanied by lot number for commercially available drug products – meaning 454 of those deaths may be associated with Novo Nordisk's FDA-approved semaglutide drugs. Again, FAERS does not indicate that Novo's drug caused the death, only that the patient was reported to have been taking that drug.

- In its public statements, Novo Nordisk repeatedly conflates compounded drugs prepared in legitimate state-licensed pharmacies with counterfeit and illicit substances available from unlicensed entities online. Those are not the same thing. The company has previously reported that its testing identified potency discrepancies and impurities in what it referred to as compounded drugs, but when asked by *The Washington Post* about the source of the substances it tested, the drugmaker declined to comment. Nor did it indicate if the tested drugs were legally acquired, how old they were when tested,

whether they'd been properly refrigerated, and whether the seal was intact on the vial before testing. Those factors affect the results of any testing. The drugmakers' ongoing conflation is germane to any effort to document claims of deaths and hospitalizations association with compounded drugs. Were the events associated with drugs prepared in state-licensed pharmacies or were they sold by illicit, unlicensed entities? We don't know, and FAERS generally does not indicate the pharmacy or facility that prepared a reported drug.

- The FAERS data does reveal that adverse events reported for compounded semaglutide largely mirror those for the FDA-approved products, suggesting that these adverse events are related to the drug itself and not the fact it was compounded or commercially manufactured.

Other Red Flags

In his comments to CNN, Mr. Jorgensen also claimed that patients taking compounded GLP1s believe they are getting semaglutide when "there's only one semaglutide, and that's produced by Novo Nordisk."

But the assertion that the API used by Novo is the "only" semaglutide is demonstrably false. FDA lists more than a dozen registered manufacturers of semaglutide on its website. While only Novo Nordisk manufactures finished-form, FDA-approved Ozempic and Wegovy, the semaglutide API that compounding pharmacies and outsourcing facilities use is sourced from those FDA-registered manufacturers and comes to the pharmacy with a certificate of analysis. In short, patients who are dispensed compounded semaglutide from a legitimate state-licensed pharmacy based on a prescription from their provider can have confidence that the compounded drug is what it says it is and has been prepared within a rigorous compliance framework focused on patient safety.

What Is and Is Not a Pharmacy

Legitimate pharmacies must be licensed in the state where the pharmacy is physically located and in all states to which the pharmacy ships compounded medications (Massachusetts is the lone exception). The best way for patients to know that the pharmacy to which their prescription is sent is legitimate is to look it up on the state board of pharmacy website in the state where the patient lives.

If it's listed there, it's licensed in that state and regulated and inspected regularly by that state's board of pharmacy.

The licensee look-up function on the board of pharmacy website in some states can be difficult to find and navigate. The Alliance for Pharmacy Compounding provides a shortcut tool called "Is it legit?" at a4pc.org/isitlegit.

Sometimes, news stories incorrectly conflate state-licensed compounding pharmacies with med spas, which are not pharmacies. That has been the case in some reporting of FDA's recent warning about improper compounding practices by a California-based entity called Fullerton Wellness. Although referenced in some media reports as a compounding pharmacy, Fullerton Wellness is not listed as a licensed pharmacy on the California Board of Pharmacy website. It's likely that it is a wellness spa, not a pharmacy, and is overseen by a physician, not a pharmacist. Physicians are authorized to oversee in-clinic compounding in most states, but it is a practice not as well-regulated and compliant with compounding standards of the U.S. Pharmacopeia as it should be.

The Proper Role of Compounded Drugs

Compounding is authorized in the Food, Drug & Cosmetic Act and through FDA Guidance in two circumstances:

- When a prescriber judges that no available FDA-approved drug is APPROPRIATE for a particular patient, a custom-made compounded drug may be prescribed. It might be a different dosage form or strength or a drug combination that is not commercially available.
- When the appropriate FDA-approved drug is not ACCESSIBLE to the patient, pharmacies may prepare copies of that drug. Specifically, pharmacies are authorized to prepare copies of FDA-approved drugs when the FDA-approved drug appears and "currently in shortage" on the FDA Drug Shortage List.

Novo Nordisk's semaglutide injection drugs have been listed as "currently in shortage" since March 2022. During this period when the drugmaker is unable to meet demand, compounding pharmacies across America are providing patients access to life-changing GLP1s like semaglutide prepared to the high standards of state regulations and the U.S. Pharmacopeia in state-licensed and inspected sterile compounding labs.

The Alliance for Pharmacy Compounding is the industry trade association and the voice for pharmacy compounding, representing more than 600 compounding small businesses – including compounding pharmacists and technicians in both 503A and 503B settings, as well as prescribers, educators, researchers, and suppliers. ***Learn more, at compounding.com or a4pc.org.***

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