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Alliance for Pharmacy Compounding

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June 20, 2024

Anthony Rubinaccio
Executive Director
New Jersey Board of Pharmacy
124 Halsey St, 6th Floor
Newark, NJ 07102

Dear Executive Director Rubinaccio and Members of the Board of Pharmacy:

I am writing to provide perspective to the Board on the Board's recently expressed concerns about compounding of sublingual forms of semaglutide.

As you may know, the Alliance for Pharmacy Compounding is the voice for pharmacy compounding, representing more than 500 compounding small businesses – including compounding pharmacists and technicians in both 503A and 503B settings – as well as prescribers, educators, researchers, and suppliers.

The New Jersey Board of Pharmacy statement concerning semaglutide compounding released in November 2023 states that the Board intends to follow FDA Guidance regarding circumstances under which a 503A compounding pharmacy can compound "essentially a copy" of an FDA-approved product. The guidance provides three criteria for determining if a human compounded medication is a copy of a commercially available drug product:

- The compounded drug product has the same active pharmaceutical ingredient(s) (API) as the commercially available drug product;
- The API(s) have the same, similar, or an easily substitutable dosage strength; and
- The commercially available drug product can be used by the same route of administration as prescribed for the compounded drug.

Compounding a semaglutide sublingual formulation via the crushing of Rybelsus tablets is not creating a copy of an FDA-approved medication, as defined by the FDA guidance.

Rather, the compounding of sublingual semaglutide – based on the judgment of the prescriber that the compounded preparation is what is needed to meet the patient's need – is a legitimate compounding practice rooted in the Food, Drug and Cosmetic Act.

In this instance, the commercially available drug product is not indicated for and cannot be used via a sublingual route of administration. The strength of the formulation, which is expressed as mg/ml, is not the same, similar, or easily substitutable dosage strength. The doses written for by prescribers as described to us by our members are not within 10 percent of the dosages offered by the commercially available products. Moreover, following FDA's 503A copies guidance would not result in deeming a sublingual formulation as a copy of the commercially available product.

The warning on the package insert of Rybelsus to not split or crush the tablets is not due to potential toxicity of semaglutide, as would be the case for some extended-release medications that should not be crushed, such as oxycodone and diltiazem. Rather, it is printed because absorption of this low oral bioavailability drug has not been studied when the tablets are not swallowed whole.

Additionally, crushing tablets, even ones that contain this "do not crush" warning, has been done in the published literature for multiple formulations. Some medications have a coating on them that enhances their appearance or covers up a bitter taste, but otherwise have no reason to list "do not crush" on their package inserts. *The International Journal of Pharmaceutical Compounding* has published a helpful article on determining if a medication tablet is indeed appropriate for crushing.

Moreover, there is at least one USP monograph for a compounded drug preparation (lansoprazole compound oral suspension, USP) that includes directions to grind the contents of lansoprazole capsules, even though their package insert says "do not crush or chew lansoprazole delayed-release capsules." There are also published formulations for oral liquid versions of hydroxyurea and mycophenolate mofetil, which both have instructions in their package inserts not to crush.

Thank you for your attention to these matters. If APC can serve as a resource on these topics or others related to compounding, we would be happy to assist.

I await your response.

Sincerely,

Scott Brunner, CAE
Chief Executive Officer
scott@a4pc.org

**From the FDA's Essential Copy Guidance: "To focus enforcement on the most significant cases, as a matter of policy, at this time FDA does not intend to take action against a compounder for compounding a drug product that is a copy of a commercially available drug product regularly or in inordinate amounts if the compounder fills four or fewer prescriptions for the relevant compounded drug product in a calendar month."*

Uttaro E, Zhao F, Schweighardt A. Filling the Gaps on the Institute for Safe Medication Practices (ISMP) Do Not Crush List for Immediate-release Products. Int J Pharm Compd. 2021 Sep-Oct;25(5):364-371. PMID: 34623961.