CLOSER LOOK

MEMORANDUM

New FDA submission for high dose semaglutide (7.2 mg) offers potential to broaden treatment options for people with obesity – November 26, 2025

Based on the phase 3b STEP UP trial, in which semaglutide 7.2 mg led to 21% weight loss at Week 72

Novo Nordisk announced this morning that it has submitted a supplemental New Drug Application (sNDA) to the FDA for a higher dose of Wegovy (semaglutide 7.2 mg) for obesity treatment. The application is based on the phase 3b STEP UP trial (n=1,407), in which semaglutide 7.2 mg achieved weight loss of 20.7% at Week 72, compared to 17.5% with semaglutide 2.4 mg and 2.4% with placebo in people with obesity but not diabetes.

As Wegovy is one of 15 candidates that received the new Commissioner's National Priority voucher (CNPV), along with Sanofi's Tzield and Lilly's orforglipron, the review is expected within one or two months after the FDA accepts the application. The first nine candidates, which included Tzield, came out October 20, and the following six came just two weeks later on November 6. Outside the US, semaglutide 7.2 mg is also under review in the EU, with a regulatory decision expected in 1Q26. Novo Nordisk submitted a variant application in the EU for semaglutide 7.2 mg in a single-dose pen in October, and the decision for the pen is expected several quarters later in 2H26.

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Phase 3b STEP-UP trial finds semaglutide 7.2 mg confers ~3 percentage point greater weight loss than the 2.4 mg dose

The sNDA is based on the phase 3b STEP UP trial (n=1,407), which compared high-dose semaglutide 7.2 mg to semaglutide 2.4 mg and placebo in people with overweight or obesity without T2D. Topline results were announced in January 2025, and full results were presented at ADA 2025. We continue to wonder about the ethics of placebo-controlled trials in an environment with so many approved medicines, and look forward to learning more on this subject. Given how well many trial groups have been doing in comparison to the placebo, we're not surprised to see engagement in clinical trials go up - while historically, placebo groups were safer, now the converse almost appears to be true, with huge benefit to be seen in the treated cohorts compared to no intervention at all.

Assuming all participants adhered to treatment, semaglutide 7.2 mg achieved weight loss of 20.7% at Week 72, compared to 17.5% with semaglutide 2.4 mg and 2.4% with placebo, from a mean baseline body weight of 113 kg (249 lbs). Moreover, one-third of people treated with semaglutide 7.2 mg achieved a weight loss of ≥25%, compared to 16.7% with semaglutide 2.4 mg and none with placebo. When applying the treatment policy estimand, people treated with semaglutide 7.2 mg achieved weight loss of 18.7%, compared to 15.6% with semaglutide 2.4 mg and 3.9% with placebo. Ultimately, this level of weight loss - with one-third reaching ≥25% - positions semaglutide 7.2 mg as a potentially transformative option for patients not yet happy with the maximum approved dose and continue to seek substantial, durable weight reduction with semaglutide.

Interestingly, from a tolerability perspective, not all participants reached the maximum tolerated dose in the trial. 75% reached the maximum dose in the semaglutide 7.2 mg group, compared to 89% for 2.4 mg and 97% for placebo. The safety and tolerability events were more common in the 7.2 mg group, as well. 71% of those taking semaglutide 7.2 mg

experienced GI side effects, compared to 61% with semaglutide 2.4 mg and 43% with placebo. Discontinuation rates were 3.3%, 2.0%, and none, respectively. Given the concerns about those in the placebo group suspecting participation in the semaglutide group and not reaching the maximum dose, these data demonstrating low discontinuation with the highest dose are positive.

Novo Nordisk's pursuit for high dose semaglutide sparks clinical consideration for titration scheme

Of note, in the STEP-UP trial, participants reached 7.2 mg through a dose escalation from 0.25 mg to 0.5 mg, 1.0 mg, 1.7 mg, 2.4 mg, and 7.2 mg every four weeks. We applaud what appears to be relatively slow and careful titration for a trial lasting just under 18 months.

At ADA 2025, several sessions emphasized the importance of personalizing obesity management. In the full results readout of phase 3 REDEFINE 1 trial (n=3,417), which evaluated CagriSema (a fixed combination of cagrilintide 2.4 mg and semaglutide 2.4 mg) in people with overweight or obesity without T2D, panelists highlighted that only 57% of trial participants stayed on high dose of CagriSema, as trial participants were allowed flexible titration. Panelists emphasized that, given the heterogeneous nature of obesity, it is important to tailor the dosage and titration schedule to achieve individual goals (see Q&A for more). Likewise, in the symposium addressing the new Standards of Care for obesity treatments, Dr. Aronne shared frustration that insurance companies often only cover the maximum approved dosage for the maintenance phase. He is hopeful that recommending any dose – whichever works best for patients – to be used for the maintenance phase in the Standards of Care could push for better insurance coverage. As Novo Nordisk seeks approval for high dose semaglutide, we are curious about its efforts to better elucidate personalized titration scheme to meet various patient needs.

High-dose semaglutide submitted in the EU, UK, and more for obesity

Semaglutide 7.2 mg and its single-dose-device formulation for obesity have been submitted to the EU regulatory authorities. In July, Novo Nordisk submitted semaglutide 7.2 mg to the EMA to expand Wegovy's label. In October, Novo Nordisk further submitted a variant application for semaglutide 7.2 mg in a single-dose pen. This submission is based on the results of the STEP UP (n=1,407) and STEP UP T2D (n=512) program presented at ADA 2025, in which semaglutide 7.2 mg achieved up to 21% weight loss across several trials. Novo Nordisk expects a regulatory decision for semaglutide 7.2 mg in early 2026 and approval of semaglutide 7.2 mg in a single-dose pen in 2H26.

In today's press announcement, Novo Nordisk also said that semaglutide 7.2 mg is under review in the UK and several other presently undisclosed countries.

Price negotiations with the US government lowers Wegovy's list price

Just yesterday, the Centers for Medicare and Medicaid Services (CMS) announced significant price discounts for 15 drugs included in the second round of Medicare Drug Price Negotiation Program (MDPNP), which will become effective on January 1, 2027. The drugs included three semaglutide products, Ozempic, Wegovy, and Rybelsus, which totaled just under $15 billion (35% of total cost) in Part D prescription costs in 2024. The negotiated price applies differently across dosage forms and strengths. Notably, Wegovy will be priced at $385.63 per 2.4 mg/0.75 mL per month, down 71% from the original list price of $1,349 per month. We imagine that the negotiated price for the high-dose semaglutide, if approved, would be similar to or higher than $385.63 per month depending on the dose concentration.

Earlier in November, the White House also announced the Most-Favored-Nation pricing for Ozempic, Wegovy, Mounjaro, and Zepbound, which would be offered at $245 per month for Medicare users with a co-pay of $50 per month, effective mid-2026. The TrumpRx direct-to-consumer platform will also allow patients to purchase Ozempic and Wegovy for $350, compared to current list prices of $1,000 and $1,350 per month, respectively, and Zepbound and orforglipron (if approved) for an average of $346 through the platform, compared to $1,086 per month.

Close Concerns' Questions

1. For what patient population does Novo Nordisk especially recommend high dose semaglutide as opposed to

semaglutide 2.4 mg?

2. How might clinicians personalize titration schemes to improve tolerability for semaglutide 7.2 mg?
3. Could patients and clinicians use intermediate doses between 2.4 mg and 7.2 mg to titrate up?
4. Will high dose semaglutide be available in single-dose pens or vials?
5. What clinician behavior related to dosage and titration schedules is helpful to optimize individual goals?

--by Kat Moon, Monica Oxenreiter, and Kelly Close