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IN BRIEF

Wegovy HD – High-Dose Injectable Semaglutide for Weight Loss

The FDA has approved *Wegovy HD*, a 7.2-mg dose of the injectable glucagon-like peptide-1 (GLP-1) receptor agonist semaglutide, for use in adults who have tolerated the 2.4-mg dose for at least 4 weeks and require additional weight reduction.

CLINICAL STUDIES – FDA approval of *Wegovy HD* was based on the results of two double-blind trials in adults with obesity (BMI ≥ 30 kg/m²).

In the first trial (STEP UP), 1407 adults with obesity without type 2 diabetes were randomized to receive semaglutide titrated to 2.4 mg or 7.2 mg or placebo SC once weekly for 72 weeks. Patients in the 7.2-mg arm were titrated directly from 2.4 mg to 7.2 mg at week 20. The mean change in weight from baseline to week 72 in the intent-to-treat population was significantly greater with the 7.2-mg dose than with the 2.4-mg dose (-18.7% vs -15.6%). More patients who received the higher dose of semaglutide achieved weight loss $\geq 5\%$ (90.7% vs 89.9%), $\geq 10\%$ (82.4% vs 75.1%), $\geq 15\%$ (66.5% vs 54.5%), $\geq 20\%$ (47.7% vs 33.3%), and $\geq 25\%$ (31.2% vs 15.3%).¹

In the second trial (STEP UP T2D), 512 adults with obesity and type 2 diabetes were randomized to receive semaglutide titrated to 2.4 mg or 7.2 mg or placebo SC once weekly for 72 weeks. The mean change in weight from baseline to week 72 in the intent-to-treat population was significantly greater with the 7.2-mg dose (-13.2% vs -10.4% with the 2.4-mg dose). More patients who received the higher dose of semaglutide achieved weight loss $\geq 5\%$ (86.3% vs 75.3%), $\geq 10\%$ (62.9% vs 51.5%), $\geq 15\%$ (41.2% vs 28.9%), and $\geq 20\%$ (21.3% vs 14.4%).²

Semaglutide vs Tirzepatide – The glucose-dependent insulinotropic polypeptide (GIP)/glucagon-like peptide-1 (GLP-1) receptor agonist tirzepatide (*Zepbound*) has been the most effective weight loss drug available to date.³ In a clinical trial in patients with obesity but not type 2 diabetes, once-weekly subcutaneous injections of tirzepatide 10-15 mg resulted in significantly greater weight loss compared to semaglutide

1.7-2.4 mg at 72 weeks in the intent-to-treat population (-20.9% vs -13.7%).⁴ No head-to-head trials are available comparing semaglutide 7.2 mg with tirzepatide 15 mg.

ADVERSE EFFECTS – In the STEP UP trials, adverse effects that occurred in $\geq 2\%$ of patients and more frequently with the 7.2-mg dose than with the 2.4-mg dose were nausea (39%), vomiting (22%), dysesthesia (22%), constipation (20%), abdominal pain (12%), fatigue (11%), headache (9%), dizziness (6%), hair loss (6%), and flatulence (4%). Discontinuation rates due to adverse effects were similar with both doses of the drug.

DOSAGE, ADMINISTRATION, AND COST – The recommended starting dosage of injectable semaglutide for chronic weight management is 0.25 mg injected subcutaneously in the abdomen, thigh, or upper arm once weekly. The label recommends titrating the dose to 0.5 mg for weeks 5-8, 1 mg for weeks 9-12, 1.7 mg for weeks 13-16, and 2.4 mg thereafter. The dose can be increased to 7.2 mg once weekly after 4 weeks in adults who require additional weight reduction. Slow titration of the dose can minimize GI adverse effects.

A one-month supply of *Wegovy HD* is available directly from the manufacturer for \$399 for self-paying patients.

CONCLUSION – The new higher dose (7.2 mg) of semaglutide (*Wegovy HD*) is more effective for weight loss than the previously approved maximum dose (2.4 mg) of the drug, but it is more likely to cause GI adverse effects and dysesthesia. Although direct comparisons are lacking, the higher dose of semaglutide appears to be almost as effective for weight loss as the maximum dose of tirzepatide (*Zepbound*). ■

1. S Wharton et al. Once-weekly semaglutide 7.2 mg in adults with obesity (STEP UP): a randomised, controlled, phase 3b trial. *Lancet Diabetes Endocrinol* 2025; 13:949.
2. I Lingvay et al. Once-weekly semaglutide 7.2 mg in adults with obesity and type 2 diabetes (STEP UP T2D): a randomised, controlled, phase 3b trial. *Lancet Diabetes Endocrinol* 2025; 13:935.
3. Drugs and devices for weight management. *Med Lett Drugs Ther* 2025; 67:121.
4. LJ Aronne et al. Tirzepatide as compared with semaglutide for the treatment of obesity. *N Engl J Med* 2025; 393:26.

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