Wegovy™ (semaglutide) – New drug approval

- On June 4, 2021, the FDA announced the approval of Novo Nordisk's Wegovy (semaglutide), as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adults with an initial body mass index (BMI) of:

    - 30 kg/m^2 or greater (obesity) or
    - 27 kg/m^2 or greater (overweight) in the presence of at least one weight-related comorbid condition (eg, hypertension, type 2 diabetes mellitus [T2DM], or dyslipidemia)

- Limitations of use for Wegovy include:

    - Wegovy contains semaglutide and should not be coadministered with other semaglutide-containing products or with any other glucagon-like peptide-1 (GLP-1) receptor agonist.
    - The safety and effectiveness of Wegovy in combination with other products intended for weight loss, including prescription drugs, over-the-counter drugs, and herbal preparations, have not been established
    - Wegovy has not been studied in patients with a history of pancreatitis.

- Semaglutide is also available under the brand name Ozempic® and Rybelsus®. Similar to Ozempic, Wegovy is administered via subcutaneous (SC) injection. Rybelsus is available as an oral tablet.

    - Ozempic is approved as an adjunct to diet and exercise to improve glycemic control in adults with T2DM and to reduce the risk of major adverse cardiovascular events in adults with T2DM and established cardiovascular disease.
    - Rybelsus is approved as an adjunct to diet and exercise to improve glycemic control in adults with T2DM.

- The efficacy of Wegovy was established in conjunction with a reduced calorie diet and increased physical activity in three 68-week, randomized, double-blind, placebo-controlled trials and one 68-week, randomized, double-blind, placebo withdrawal trial. In studies 1, 2, and 3, Wegovy or matching placebo was escalated to 2.4 mg SC weekly during a 16-week period followed by 52 weeks on maintenance dose. For these studies, the primary efficacy parameters were mean percent change in body weight and the percentages of patients achieving ≥ 5% weight loss from baseline to week 68.

    - After 68 weeks, treatment with Wegovy resulted in a statistically significant reduction in body weight vs. placebo in all three studies. The mean percent difference from placebo in body weight was -12.4 (95% CI: -13.3, -11.6) in study 1, -6.2 (95% CI: -7.3; -5.2) in study 2, and -10.3 (95% CI: -11.8; -8.7) in study 3 ($p < 0.0001$ for all).
    - In all three studies, a greater proportion of patients treated with Wegovy achieved 5% weight loss than those treated with placebo. The percentage of patients meeting this goal ranged from 67.4% to 84.8% with Wegovy vs. 30.2% to 47.8% with placebo ($p < 0.0001$ for all).

- In Study 4, Wegovy was escalated during a 20-week run-in period, and patients who reached Wegovy 2.4 mg after the run-in period were randomized to either continued treatment with Wegovy or placebo for 48 weeks. The primary efficacy parameter was mean percent change in body weight from randomization (week 20) to week 68.

    - The mean percent difference from placebo in body weight change was -14.8 (95% CI: -16.0, -13.5; $p < 0.001$).

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- Wegovy carries a boxed warning for risk of thyroid C-cell tumors.

- Wegovy is contraindicated in the following conditions:

    — A personal or family history of medullary thyroid carcinoma or in patients with multiple endocrine neoplasia syndrome type 2.
    — A prior serious hypersensitivity reaction to semaglutide or to any of the excipients in Wegovy. Serious hypersensitivity reactions, including anaphylaxis and angioedema, have been reported with semaglutide.

- Additional warnings and precautions for Wegovy include acute pancreatitis, acute gallbladder disease, hypoglycemia, acute kidney injury, hypersensitivity, diabetic retinopathy complications in patients with T2DM, increased heart rate, and suicidal behavior and ideation.

- The most common adverse reactions (≥ 5%) with Wegovy use were nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distension, eructation, hypoglycemia in patients with T2DM, flatulence, gastroenteritis, and gastroesophageal reflux disease.

- The recommended initial dose of Wegovy is 0.25 mg injected SC once-weekly. The recommended dose escalation schedule is provided in the table below to minimize gastrointestinal adverse reactions.

    — If patients do not tolerate a dose during dose escalation, delaying dose escalation for 4 weeks should be considered.
    — The maintenance dose is 2.4 mg injected SC once-weekly.
    — If patients do not tolerate the maintenance 2.4 mg once-weekly dose, the dose can be temporarily decreased to 1.7 mg once-weekly, for a maximum of 4 weeks. After 4 weeks, the dose should be increased 2.4 mg. Wegovy should be discontinued if the patient cannot tolerate the 2.4 mg dose.

Weeks	Weekly dose	
1 through 4	0.25 mg	Dose escalation
5 through 8	0.5 mg	
9 through 12	1 mg	
13 through 16	1.7 mg	
Week 17 and onward	2.4 mg	Maintenance dose

- Novo Nordisk plans to launch Wegovy later this month. Wegovy will be available as 0.25 mg, 0.5 mg, 1 mg, 1.7 mg, and 2.4 mg prefilled, single-dose pens.

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