Optum Rx®

Wegovy® (semaglutide) – New indication

- On March 8, 2024, the FDA announced the approval of Novo Nordisk's Wegovy (semaglutide), in combination with a reduced calorie diet and increased physical activity, to reduce the risk of major adverse cardiovascular events (MACE) (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke) in adults with established cardiovascular disease (CVD) and either obesity or overweight.

- Wegovy, a glucagon-like peptide-1 (GLP-1) receptor agonist, is the first FDA approved treatment to reduce the risk of MACE specifically in adults with obesity or overweight.

- Wegovy is also approved in combination with a reduced calorie diet and increased physical activity to reduce excess body weight and maintain weight reduction long term in: (1) adults and pediatric patients aged 12 years and older with obesity, and (2) adults with overweight in the presence of at least one weight-related comorbid condition.

- The approval of Wegovy for the new indication was based on the SELECT cardiovascular outcomes trial, a randomized, double-blind, placebo-controlled study in 17,604 patients with an initial body mass index (BMI) of ≥ 27 kg/m^2 and established CVD (prior myocardial infarction, prior stroke, or peripheral arterial disease). Patients were randomized to Wegovy or placebo, added to current standard of care, which included management of CV risk factors and individualized healthy lifestyle counseling. The primary endpoint, MACE, was the time to first occurrence of a three-part composite outcome which included cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke.
    - Wegovy statistically significantly reduced the risk of MACE by 20% compared to placebo when added to standard of care. The treatment effect for the primary composite endpoint, its components, and other relevant endpoints are shown in the table below.

Endpoint	Patients with events, n (%)		Hazard ratio (95% CI)
	Placebo	Wegovy	
Primary composite	701 (8.0%)	569 (6.5%)	0.80 (0.72, 0.90)*
Key secondary endpoints			
CV death†	262 (3.0%)	223 (2.5%)	0.85 (0.71, 1.01)
All-cause death‡	458 (5.2%)	375 (4.3%)	0.81 (0.71, 0.93)
Other secondary endpoints			
Fatal or non-fatal myocardial infarction§	334 (3.8%)	243 (2.8%)	0.72 (0.61, 0.85)
Fatal or non-fatal stroke§	178 (2.0%)	160 (1.8%)	0.89 (0.72, 1.11)

* p-value < 0.001
† CV death was the first confirmatory secondary endpoint in the testing hierarchy and superiority was not confirmed
‡ Confirmatory secondary endpoint. Not statistically significant based on the prespecified testing hierarchy
§ Not included in the prespecified statistical testing hierarchy

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

- The recommended initial dose of Wegovy in adults is 0.25 mg injected subcutaneously (SC) once weekly. The dose escalation schedule below should be followed to minimize gastrointestinal adverse reactions. If patients do not tolerate a dose during dosage escalation, delaying dosage escalation should be considered for 4 weeks. The maintenance dosage of Wegovy in adults is either 2.4 mg (recommended) or 1.7 mg once weekly.

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Treatment	Weeks	Once weekly SC dosage
Initiation	1 through 4	0.25 mg
Escalation	5 through 8	0.5 mg
	9 through 12	1 mg
	13 through 16	1.7 mg
Maintenance	17 and onward	1.7 mg or 2.4 mg

- Refer to the Wegovy drug label for pediatric dosing for chronic weight management.