

Prior Authorization Criteria Update: Semaglutide

Purpose: This update reviews the evidence for the use of semaglutide (WEGOVY) in patients with cardiovascular (CV) disease who are overweight or obese. Recommendations for prior authorization (PA) criteria to allow coverage of semaglutide (WEGOVY) for secondary prevention of major CV events will be presented.

Plain Language Summary:

- The Food and Drug Administration approved a medicine called semaglutide (WEGOVY) for patients with overweight or obesity who also had a history of heart disease, such as heart attacks.
- In studies, people who took semaglutide (WEGOVY) for about 3 years had a reduction in death due to heart disease and fewer heart attacks or strokes compared to people who took a product that contained no medication (saline injection).
- The most common side effects of semaglutide were nausea and diarrhea.
- People stopped taking semaglutide because of side effects more often than people taking placebo.
- The Oregon Health Plan (OHP) does not currently pay for semaglutide (WEGOVY) for people living with overweight or obesity if they do not also have a history of cardiovascular disease or diabetes. OHP can pay for semaglutide (WEGOVY) when it is prescribed to people with overweight or obesity who also have a history of heart disease.
- Before paying for semaglutide, we recommend that OHP verify that it is prescribed for people who:
 - Have heart disease and
 - Live with overweight or obesity and
 - Are engaged in diet and exercise lifestyle changes.

Semaglutide received an indication in March 2024, in combination with reduced calorie diet and increased physical activity, to reduce the risk of major CV events (e.g., CV death, non-fatal myocardial infarction [MI], or non-fatal stroke) in adults with established CV disease and either obesity or overweight.¹ The evidence to support this indication was from one double-blind, placebo-controlled, phase 3, randomized trial (SELECT) (**Table 2**).²

In the SELECT trial, 17,604 patients were randomized to semaglutide or placebo (**Table 1**). Adults 45 years and older with a BMI of 27 kg/m² or greater and established CV disease were required for inclusion.² Patients with diabetes were excluded. Doses of semaglutide were injected subcutaneously weekly, initiated at 0.24 mg and increased every 4 weeks (0.5 mg, 1.0 mg, 1.7 mg, 2.4 mg). The target dose was 2.4 mg weekly, which was obtained by 77% of patients at 104 weeks.² Key baseline characteristics of adults enrolled in the SELECT trial are presented in **Table 1**.

Table 1. Key Baseline Characteristics of Patients Enrolled in the SELECT Trial²

Characteristic	Results (n=17,604)	Comments
Mean Age	62 years	Older than most Medicaid FFS members
Male	72.3%	Female demographic under-represented
Mean BMI	33.3 kg/m ²	Overweight population under-represented
Obese (>30 kg/m ² BMI)	71.5%	Results most applicable to patients who have obesity
Cardiovascular Inclusion Criteria		
Myocardial infarction only	67.6%	N/A
Stroke only	17.8%	N/A
Peripheral arterial disease	4.45%	N/A
Cardiovascular Medications		
Acetylsalicylic acid	78.2%	N/A
P2Y12 receptor inhibitors	33.7%	N/A
Lipid lowering drugs	90.1%	N/A
Beta-blockers	70.2%	N/A
ACE-inhibitors	45%	N/A
ARBs	29.5%	N/A

Abbreviations: ACE = angiotensin-converting-enzyme; ARB = angiotensin- receptor blocker; BMI = body mass index; FFS = fee-for-service; N/A = not applicable

There is moderate strength of evidence that semaglutide reduces the composite endpoint of risk of death from CV causes, nonfatal MI or nonfatal stroke, compared to placebo, in adults with CV disease and have overweight or obesity (**Table 2**).² Sixty-seven people would need to be treated for 3.3 years to prevent one CV event (absolute risk reduction [ARR] 1.5%/number needed to treat [NNT] 67).² Secondary endpoints were evaluated in hierarchical order starting with death from CV causes, which did not meet statistical significance (HR 0.85; 95% CI, 0.71 to 1.01; p=0.07). Therefore, the other secondary outcomes did not have superiority testing performed. Results reported for secondary outcomes were based on point estimates and 95% confidence intervals. The width of the confidence intervals was not adjusted for multiplicity and should not be used to determine treatment effects.²

Table 2. Evidence for the Use of Semaglutide in Adults with CV Disease

Lincoff, et al ² (SELECT Trial) DB, PC, Phase 3, RCT	Semaglutide 2.4 mg subcutaneously weekly Vs.	Adults with CV disease, and BMI of 27 kg/m ² or greater and no diabetes (n=17604)	Composite of death from CV causes, nonfatal MI or nonfatal stroke	CV end-point event: Semaglutide: 569 (6.5%) Placebo: 701 (8.0%) HR 0.80 (95% CI, 0.72 to 0.90) P<0.001	Mean duration of exposure was 34.2 months, mean age was 61.6 years, 73% male, and 84% White. Mean bodyweight was a BMI of 33 kg/m ² . Individual components of composite endpoint were not
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	Placebo			ARR 1.5%/NNT 67	statistically different between semaglutide and placebo. Sixty-seven people would need to be treated for approximately 34 months to prevent one CV event.
	Mean follow-up: 39.8 months			<u>Secondary Endpoints:</u> Body weight change at 104 weeks: Semaglutide: -9.39% Placebo: -0.88% MD -8.51% (95% CI, -8.75 to -8.27)	

Abbreviations: ARR = absolute risk reduction; BMI = body mass index; CV = cardiovascular; DB = double-blind; MI = myocardial infarction; NNT = number needed to treat; PC = placebo-controlled; RCT = randomized controlled trial

The most common adverse reactions in patients randomized to semaglutide are nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, and dizziness. Seventeen percent of patients discontinued semaglutide due to adverse events compared to 8% of patients taking placebo (p<0.001).²

Tirzepatide is also currently being evaluated in an ongoing trial for prevention of CV outcomes.³

Recommendation:

- Implement PA criteria for semaglutide (WEGOVY) (**Appendix 1**).
- Evaluate costs in executive session.

References:

1. Wegovy (semaglutide) [prescribing information]. Plainsboro, NJ; Novo Nordisk Inc. March 2024.
2. Lincoff AM, Brown-Frandsen K, Colhoun HM, et al. Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes. *N Engl J Med*. 2023;389(24):2221-2232. doi:10.1056/NEJMoa2307563
3. A Study of Tirzepatide (LY3298176) Compared to Dulaglutide on Major Cardiovascular Events in Participants with Type 2 Diabetes (SURPASS-CVOT). ClinicalTrials.gov identifier: NCT04255433. Updated February 21, 2022. Accessed April 3, 2024.

Appendix 1. Proposed Prior Authorization Criteria

Weight Management Drugs for Secondary Cardiovascular Prevention

Goal(s):

- To provide guidance for the use of weight management drugs, like semaglutide (WEGOVY), to ensure coverage for the most appropriate patient populations in which evidence supports efficacy and safety for reduction in cardiovascular (CV) outcomes.

Length of Authorization:

- Up to 6 months

Requires PA:

- All doses of semaglutide (WEGOVY) require PA.

Note: Semaglutide is not currently covered for people who do not have established cardiovascular disease or diabetes.

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the request for an FDA-approved indication?	Yes: Go to #3	No: Pass to RPh. Deny; medical appropriateness.
3. Is the request for continuation of therapy?	Yes: Go to Renewal Criteria	No: Go to #4
4. Does the patient have a BMI of 27 kg/m ² or greater?	Yes: Go to #5 Document current BMI	No: Pass to RPh. Deny; medical appropriateness.
5. Does the patient have established cardiovascular disease (e.g., history of myocardial infarction, stroke, or symptomatic peripheral arterial disease)?	Yes: Go to #6	No: Deny; medical appropriateness

Approval Criteria

6. Is the patient enrolled in a lifestyle modification program that includes a reduced calorie diet and regular physical activity?	Yes: Approve for up to 6 months to allow for titration. Medication supply is subject to quantity limits.	No: Deny; medical appropriateness
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Renewal Criteria

1. Is the request for continuation of therapy that has been previously approved?	Yes: Go to #2	No: Go to Approval Criteria
2. Has the patient lost or maintained a BMI reduction of 5% or more?	Yes: Go to #3	No: Deny; medical appropriateness
3. Is the patient continuing with a lifestyle modification program that includes a reduced calorie diet and regular physical activity?	Yes: Approve for up to 12 months. Medication supply is subject to quantity limits.	No: Deny; medical appropriateness

P&T/DUR Review: 6/24 (KS)

Implementation: TBD