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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/m^2 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**.

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Table 1. Key Baseline Characteristics of Patients Enrolled in the SELECT Trial[2]

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

	Placebo Mean follow-up: 39.8 months			ARR 1.5%/NNT 67 <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)	statistically different between semaglutide and placebo. Sixty-seven people would need to be treated for approximately 34 months to prevent one CV event.
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). Clinical Trials.gov identifier: NCT04255433. Updated February 21, 2022. Accessed April 3, 2024.

Appendix 1. Proposed Prior Authorization Criteria

Weight Management Drugs

Goal(s):

- To provide guidance for the use of weight management therapies to ensure they are used in the most appropriate patient populations in which evidence supports efficacy and safety.
- Allow case-by-case review for members covered under the EPSDT program. Recommend use of GLP-1 receptor agonists only for FDA-approved indications supported by the evidence.
- 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
- Renewal up to 12 months

Requires PA:

- All drugs used for weight management.
- All doses of semaglutide (WEGOVY) require PA.
- Refer to the Glucagon-like Peptide-1 (GLP-1) Receptor Agonists and Glucose Dependent Insulinotropic Polypeptide (GIP) Receptor Agonist PA Criteria for approval of Semaglutide (OZEMPIC and RYBELSUS) for type 2 diabetes.

  Note: Semaglutide is not currently covered for adults who do not have established cardiovascular disease or type 2 diabetes.

Table 1. Drugs FDA Approved for Weight Management

Drug	Adults	Pediatrics
Liraglutide (SAXENDA)	Yes	Yes – 12 years and older
Naltrexone/bupropion (CONTRAVE)	Yes	No
Phentermine/topiramate (QSYMIA)	Yes	Yes – 12 years and older
Semaglutide (WEGOVY)	Yes	Yes – 12 years and older
Tirzepatide (ZEPBOUND)	Yes	No
Setmelanotide (IMCIVREE)	Yes	Yes – 6 years and older
Orlistat (Xenical)	Yes	Yes – 12 years and older

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org

- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Table 2. BMI Cutoffs for Obesity by Sex and Age for Pediatric Patients Aged 12 Years and Older (CDC Criteria)

Age (years)	Body mass index (kg/m2) at 95% percentile	
	Males	Females
12	24.2	25.2
12.5	24.7	25.7
13	25.1	26.3
13.5	25.6	26.8
14	26.0	27.2
14.5	26.4	27.7
15	26.8	28.1
15.5	27.2	28.5
16	27.5	28.9
16.5	27.9	29.3
17	28.2	29.6
17.5	28.6	30

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is requested medication for a patient less than 21 years of age and 6 years of age or older?	**Yes:** Go to #3	**No:** Go to #12
3. Is this a request for continuation of therapy after an initial approval by FFS?	**Yes**: Go to renewal criteria	**No:** Go to #4
4. Is this an FDA approved indication?	**Yes**: Go to #5	**No:** Pass to RPh. Deny; medical appropriateness
5. Is the request for setmelanotide?	**Yes**: Go to #6	**No:** Go to #8

Approval Criteria		
6. Does the patient have obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency confirmed by genetic testing demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance OR does the patient have Bardet—Biedl syndrome (BBS)?	**Yes**: Go to #7	**No:** Deny; medical appropriateness.
7. Does the patient have a history of depression and/or suicidal ideation?	**Yes**: Deny; medical appropriateness.	**No:** Approve for up to 6 months.
8. Does the patient have a BMI corresponding to 30 kg/m^2 or $\geq$27 kg/m^2 and comorbid conditions [e.g., diabetes mellitus, hypertension, dyslipidemia, or cardiovascular disease] for adults or a BMI at the 95th percentile or greater for age and sex (Table 2 above)?	**Yes:** Go to #9 Record baseline BMI	**No:** Deny; medical appropriateness
9. Does the patient have comorbidities (e.g., hypertension, dyslipidemia, diabetes, fatty liver disease, depression, or sleep apnea)?	**Yes:** Go to #11	**No:** Go to #10
10. Has the patient previously tried a weight loss treatment plan administered by a health care provider (e.g., diet and exercise program, nutritional counseling, and/or a calorie restricted diet) for a time period of at least 3 months within the previous 6 month timeframe*? * See Clinical Notes Below	**Yes:** Go to #11	**No:** Deny; medical appropriateness. Lifestyle modifications are recommended by guidelines.
11. Will the patient be engaged in a weight management lifestyle modification program in addition to pharmacotherapy?	**Yes:** Approve for 6 months.	**No:** Deny; medical appropriateness. All drugs approved for weight loss are indicated as an adjunct to diet and exercise.

Approval Criteria		
12. Is the request for a weight management drug with an FDA-approved indication for secondary cardiovascular prevention?	**Yes:** Go to #13	**No:** Pass to RPh. Deny; drugs are not covered by OHP for adults when indicated for weight loss.
13. Is the request for continuation of therapy previously approved by FFS?	**Yes:** Go to Renewal Criteria	**No:** Go to #14
14. Has the patient been screened for diabetes within the past year AND do results indicate they do not have diabetes (e.g., HbA1c <6.5% or fasting blood glucose <126 mg/dl (7 mmol/L)?	**Yes:** Go to #15	**No:** Pass to RPh; Deny; medical appropriateness. Recommend a GLP-1 RA indicated for glucose lowering (see GLP-1 RA/GIP RA PA criteria)
15. Is the patient 45 years of age or older?	**Yes:** Go to #16	**No:** Pass to RPh. Deny; medical appropriateness.
16. Does the patient have a BMI of 27 kg/m^2 or greater?	**Yes**: Go to #17 Document current BMI	**No:** Pass to RPh. Deny; medical appropriateness.
17. Does the patient have established cardiovascular disease (e.g., history of myocardial infarction, stroke, or symptomatic peripheral arterial disease)?	**Yes**: Go to #18	**No:** Deny; drugs are not covered by OHP for adults when indicated for weight loss.
18. Has the patient previously tried a weight loss treatment plan administered by a health care provider (e.g., diet and exercise program, nutritional counseling, and/or a calorie restricted diet) for a time period of at least 3 months within the previous 6 month timeframe?	**Yes**: Go to #19	**No:** Deny; medical appropriateness

Approval Criteria		
19. Is the patient currently taking semaglutide (Ozempic) 2.0 mg weekly and is able to tolerate the medication and is still desiring additional weight loss?	**Yes**: Approve for up to 6 months	**No:** Go to #20
20. Will the patient try semaglutide (Ozempic) for at least 6 months to ensure tolerability/compliance?	**Yes**: Approve Ozempic for up to 6 months	**No:** Pass to RPh. Deny; medical appropriateness.

Renewal Criteria		
1. Is this a request for continuation of therapy with a weight loss medication previously approved by FFS?	**Yes**: Go to #2	**No:** Go to **Approval Criteria** above
2. Is the person requesting the medication less than 21 years of age?	**Yes:** Go to #3	**No:** Go to #4
3. Has the patient lost at least 1% of BMI from baseline or maintained at least a 1% BMI weight loss?	**Yes:** Go to #7	**No:** Deny; medical appropriateness
4. Is the request for ongoing treatment for someone with established cardiovascular disease (e.g., history of myocardial infarction, stroke, or symptomatic peripheral arterial disease)?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; drugs are not covered by OHP for adults when indicated for weight loss.
5. Has the patient lost or maintained a BMI reduction of 5% or more?	**Yes**: Go to #6	**No:** Deny; medical appropriateness
6. Has the patient been adherent to therapy based on provider attestation?	**Yes:** Go to #7	**No:** Deny; medical appropriateness

Renewal Criteria		
7. Is the patient continuing with a weight loss treatment plan (e.g., diet and exercise program, nutritional counseling, and/or a calorie restricted diet)?	**Yes:** Approve for up to 12 months.	**No:** Deny; medical appropriateness. All drugs approved for weight loss are indicated as an adjunct to diet and exercise.

***Clinical Notes**

Adapted from the following guideline on the treatment of adolescents with obesity:

- American Academy of Pediatrics. *Pediatrics*. 2023;151(2): e2022060640. Available at: https://publications.aap.org/pediatrics/article/151/2/e2022060640/190443/Clinical-Practice-Guideline-for-the-Evaluation-and?autologincheck=redirected

Recommended Behavior Strategies	
Strategy	**Description**
1. Reduction in sugar-sweetened beverages (SSBs)	Higher intake of sugar-sweetened beverages (carbonated beverages, sweetened beverages, soda, sports drinks, and fruit drinks) is associated with greater weight gain in adults and children. The American Heart Association (AHA) recommends not more than 25 g (6 tsp) each day of added sugar and not more than 1, 8-oz serving of SSB per week. The AAP discourages the consumption of sports drinks and energy drinks for children and adolescents. The AAP statement on fruit juice notes that it is a poor substitute for whole fruit because of its high sugar and calorie content and pediatricians should advocate for elimination of fruit juice in children with excessive weight gain.

2. Choose My Plate	MyPlate is the US Department of Agriculture's (USDA) broad set of recommendations for healthy eating for Americans. These recommendations include multiple healthy diet goals: low in added sugar, low in concentrated fat, nutrient dense but not calorie dense, within an appropriate calorie range without defined calorie restriction, and with balanced protein and carbohydrate. The principles can be adapted to different food cultures. There is a surprising dearth of literature on the impact of these guidelines on health and BMI outcomes and on the most effective education practices. **Available at: USDA choose my plate.gov**
3. 60 minutes daily of moderate to vigorous physical activity	Aerobic exercise, especially for 60 min at a time, is associated with improved body weight in youth although its effect may be small and variable. It is also associated with better glucose metabolism profiles. High-intensity interval training in youth with obesity may improve body fat, weight, and cardiometabolic risk factors, although the effect is variable. The Physical Activity Guidelines for Americans recommends 60 min per day for children and adolescents.
4. Reduction in sedentary behavior	Reduction in sedentary behavior, generally defined as reduced screen time, has consistently shown improvement in BMI measures, although impact is small. Early studies focused on reduced television, a discrete activity that is simpler than current multifunctional electronic devices. The AAP recommends no media use under age 18 month, a 1-hour limit for ages 2–5 years, and a parent- monitored plan for media use in older children, with a goal of appropriate, not- excessive use but without a defined upper limit.
The activities most commonly associated with positive behavior change are: parental involvement in goal setting, problem solving, social support, demonstrating desired behaviors, and home environment modifications to support positive change.	
Abbreviations: AAP – American Academy of Pediatrics; BMI = body mass index; oz = ounce; tsp = teaspoon; USDA = United States Department of Agriculture	