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Prior Authorization Criteria Update: Semaglutide

Purpose of Update:

The purpose of this prior authorization (PA) update is to evaluate evidence for recurrent cardiovascular events in people less than 45 years of age. This information may be used to inform recommendations for semaglutide coverage in this population.

Plain Language Summary:

- The Food and Drug Administration has approved a medicine called semaglutide (or Wegovy®) in people who live with overweight or obesity and have either heart disease or damaged blood vessels (vascular disease).
- Semaglutide was studied in people over 45 years old with overweight or obesity and heart disease or vascular disease. In people who took semaglutide for about 3 years, 6.5% of people had another heart attack, stroke or died compared to 8% of people who did not take semaglutide. Semaglutide has not been studied in younger people with heart disease, but studies indicate that young people with heart disease have high risk for a repeated heart attack, stroke, or death.
- Several health organizations recommend treatment for overweight or obesity in people with heart or vascular disease to decrease their risk for heart attack, stroke or death. They recommend diet, exercise, and medicines like semaglutide.
- Semaglutide is not covered under the Oregon Health Plan fee-for-service program in people between 21 and 45 years old with overweight or obesity and heart or vascular disease. Coverage of semaglutide for these people is recommended because they are at increased risk for recurrent heart attack, stroke or death.

Conclusions:

- Trials that evaluated semaglutide for secondary prevention of cardiovascular (CV) events in people with overweight or obesity and CV disease were limited to participants older than 45 years of age.[1] There is currently no evidence that safety or adverse effects of semaglutide vary by age.
- In people with risk factors for CV disease, guidelines recommend risk stratification to estimate risk for major adverse CV events (MACE). Most guidelines categorize people with established CV disease as having high risk for recurrent MACE. Definitions for high risk vary based on the guideline, but range from a 10-year risk of 10% to over 30%.[2-4] Guidelines from the American Heart Association/American College of Cardiology (AHA/ACC) and the Scottish Intercollegiate Guideline Network (SIGN) emphasize that use of any single risk factor, such as age or individual test results, is insufficient to adequately stratify risk of patients.[3,4] Instead, they recommend evaluation of a combination of clinical factors.[3]
- Limited data from observational studies indicate that people with premature CV disease (<45 years of age) have similar risk for recurrent MACE as older populations.[5,6] Risk factors contributing to CV events may differ based on age with a higher prevalence of substance use disorders in younger patients with CV disease.[6,7]

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- Obesity is a primary risk factor for MACE, and guidelines consistently recommend weight management to decrease risk for recurrent events in people with CV disease.[2-4,8,9] Recommendations for weight management generally include lifestyle modifications (diet, exercise, and behavioral changes) and drug therapy (including semaglutide) when lifestyle changes are insufficient to meet weight loss goals.

Recommendations:

- Remove age restrictions for semaglutide in people with established CV disease with overweight or obesity because this population is at increased risk of recurrent MACE independent of age.

Prior Reviews and Current Policy:

Semaglutide has been approved by the Food and Drug Administration (FDA) for the following indications:

- To improve glycemic control in people with type 2 diabetes (Ozempic® or Rybelsus®) or reduce risk of major adverse CV events (MACE) in adults with type 2 diabetes and established CV disease (Ozempic®).
- In combination with diet and exercise, to reduce weight or maintain weight reduction in 1) overweight with at least one weight-related comorbidity or 2) obesity (Wegovy®).
- In combination with diet and exercise, to reduce risk of MACE in adults with established CV disease and either obesity or overweight (Wegovy®).

Evidence for these indications has been previously reviewed by the Pharmacy and Therapeutics (P&T) Committee. In the fee-for-service program, semaglutide requires PA and is covered in people with 1) type 2 diabetes mellitus who are on metformin; or 2) overweight or obesity if younger than 21 years of age; and 3) established CV disease (e.g., peripheral artery disease, non-fatal myocardial infarction [MI], or non-fatal stroke) if older than 45 years of age with obesity or overweight. The evidence to support secondary CV prevention was from one double-blind, placebo-controlled, phase 3, randomized trial (called SELECT) which enrolled people who were over 45 years of age with established CV disease (most of whom were on other guideline directed therapy). [1] Semaglutide 2.4 mg weekly reduced risk of death from CV causes, non-fatal MI, or non-fatal stroke by 1.5% over a mean follow-up of 39.8 months (number needed-to-treat of 67 persons over about 3.3 years).[1] Overall risk for the composite endpoint was 6.5% with semaglutide compared to 8% with placebo (hazard ratio [HR] 0.80; 95% confidence interval [CI] 0.72 to 0.90).[1] Details of this trial were recently evaluated by the P&T Committee in June 2024.

Drugs prescribed for weight loss are currently excluded from the Oregon Medicaid state plan. The P&T Committee recommended that the Oregon Health Authority (OHA) identify a funding plan before covering drugs when prescribed for weight management. However, when drugs are prescribed for indications other than weight loss, they are required to be covered on the Oregon Medicaid plan when there is sufficient evidence for efficacy and safety. Utilization can be limited to medically appropriate use for FDA-approved or compendia-supported indications. Current off-label, compendia-supported indications for semaglutide include obesity in people who have heart failure with preserved ejection fraction and non-alcoholic (also called metabolic-associated) steatohepatitis (NASH or MASH). An update to the Medicaid state plan is not required for coverage of compendia-supported indications.

Methods:

A Medline literature search was conducted for new systematic reviews and RCTs assessing cardiovascular risk and efficacy of semaglutide in people less than 45 years of age compared to older populations. The OHSU Drug Effectiveness Review Project, Cochrane Collaboration, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, the Canadian Agency for Drugs and Technologies in Health (CADTH), and the Scottish Intercollegiate Guidelines Network (SIGN) resources were manually searched for high quality and relevant systematic reviews or guidelines. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources. If there is inadequate data from randomized controlled trials, observational studies may be evaluated.

Risk Assessment for Cardiovascular Disease

Primary Prevention

CV disease is the leading cause of death in the United States (US). CV disease encompases both heart disease and vascular disease. The most common type of heart disease in the US is coronary artery disease. In 2021, one in every 5 deaths was attributed to CV disease.[10] Prevalence of CV disease, particularly coronary artery disease, increases with age. From 2015 to 2018 in people with coronary artery disease, less than 1% were 20 to 39 years of age, 7% of people were 40 to 59 years of age, and 92% of people were 60 years and older.[3] Several factors have been associated with heart disease. Key modifiable risk factors for coronary artery disease include hyperlipidemia, hypertension, and smoking.[10] Other traditional risk factors include diabetes mellitus, overweight and obesity, physical inactivity and excessive alcohol use. Several studies have assessed the importance of these risk factors on heart disease. Based on data from the INTERHEART study, the SIGN guidelines for CV disease describe 9 risk factors which accounted for more than 90% of risk for MI. These risks include smoking, history of hypertension or diabetes, waist to hip ratio, dietary patterns, physical activity, alcohol consumption, blood apolipoproteins, and psychosocial factors.[4] They also report that smoking, blood pressure and cholesterol may account for 90% of attributable risk of coronary artery disease.[4] The US Preventative Services Task Force (USPSTF) highlighted similar risk factors, including older age, male sex, high blood pressure, current smoking, abnormal cholesterol levels, diabetes, obesity, and physical inactivity.[11] A Cochrane review identified risk factors for coronary artery disease and stroke and reported similar findings, including abnormal cholesterol, elevated blood pressure, diabetes mellitus, smoking, unhealthy diet, excessive alcohol intake, abdominal obesity, psychosocial stress, and lack of physical activity.[12]

Most guidelines, including those from the AHA/ACC, recommend quantifying potential risk for MACE in people who have risk factors for atherosclerotic cardiovascular disease (ASCVD). Several risk assessment tools have been developed to quantify the risk of MACE. In people without CV disease, the Framingham Risk Score and Pooled Cohort Equations are some of the most commonly used risk calculators in the US. Definitions for high, intermediate, or low risk categories vary slightly depending on the guideline. In people without established CV disease, the NICE defines high risk groups as having greater than 10% risk of MACE over a 10 year period.[2] The Scottish Intercollegiate Guidelines Network,[4] Framingham Heart Study[13] and Pooled Cohort Equations[13] define high risk as more than 20% risk of MACE over 10 years.

Guidelines emphasize that testing alone or use of any single risk factor is insufficient to adequately stratify risk of patients.[3,4] Instead they recommend evaluating a combination of clinical factors and testing which demonstrates improved accuracy of predictive models in clinical trials.[3] In 2018, the USPSTF concluded that there was insufficient evidence to assess the balance of benefits and harms of adding the ankle-brachial index, high-sensitivity C-reactive protein level, or coronary artery calcium score to traditional risk assessment tools for CV disease in asymptomatic adults.[11] An update of this guideline is currently in progress. They also found inadequate evidence to determine whether adding resting or exercise electrocardiogram testing to conventional risk factor assessments leads to improved risk stratification or changes treatment decisions.[13] For asymptomatic adults at intermediate or high risk for MACE, there is insufficient evidence to determine whether information from the electrocardiogram results in a change in risk management and ultimately reduces CV events.[13] Guidelines published in 2021 from the Canadian Cardiovascular Society recommend testing for lipoprotein(a) once per lifetime to inform need for intensive dyslipidemia management.[14] Use of coronary artery calcium screening is suggested in the primary prevention setting for people at intermediate risk for cardiovascular disease (10-20% 10-year risk) when the decision to prescribe statin therapy is uncertain.[14]

Secondary Prevention

Most guidelines automatically categorize people with established CV disease as having high or very high risk for recurrent MACE. For example, guidelines on prevention of stroke from SIGN note a significant risk following an initial stroke or transient ischemic attack (26% within 5 years of a first stroke and 39% by 10 years).[15] Because a prior CV event is a major risk factor for recurrent events, different risk calculators have been developed for people who have established CV disease. Guidelines from the AHA/ACC recommend stratification of patients with chronic coronary artery disease into low (<1%), intermediate (1-3%), or high (>3%) *annual* risk for CV death or non-fatal MI.[3] Stratification should be based on diagnostic testing or validated risk scores. The AHA/ACC highlight that people with a history of multiple major ASCVD events or people with a major ASCVD event and with 2 or more high-risk conditions are at very high risk for recurrent MACE. Major ASCVD events were defined as acute coronary syndrome within past 12 months, history of other MI, history of ischemic stroke, or symptomatic peripheral artery disease (history of claudication with ankle-brachial index less than 0.85, prior revascularization or amputation).[3] High-risk conditions were defined as age greater than or equal to 65 years, familial hypercholesterolemia, prior coronary artery bypass graft surgery or percutaneous coronary intervention outside of a major ASCVD event, diabetes, hypertension, chronic kidney disease (estimated glomerular filtration rate [eGFR] of 15-69 mL/min/1.73m^2), current smoking, low density lipoprotein greater than or equal to 100 mg/dL while on max tolerated statin/ezetimibe, and congestive heart failure.[3]

Currently available tools which have been developed and validated specifically for people with established CV disease include the SMART risk score and REACH registry risk estimates. These models incorporate a variety of factors to estimate risk for recurrent events. Factors included in the SMART risk score are age, sex, diabetes, current smoking status, systolic blood pressure, total cholesterol, HDL cholesterol, high-sensitivity C-reactive protein, eGFR, years since the first CV event, and type of CV disease (e.g., stroke, coronary artery disease, abdominal aortic aneurysm, or peripheral artery disease).[16] Predictive factors for CV risk included in the REACH registry score are sex, age, current smoking, diabetes mellitus, CV disease burden (i.e., number of vascular beds involved), MACE in the past year, heart failure, and atrial fibrillation.[17] Protective factors identified in the REACH registry included body mass index (BMI) less than 20 kg/m^2 and presence of medications, specifically statins and aspirin, which decreased risk of MACE.[17] Overall, these models appear to have modest ability to accurately predict recurrent MACE. Upon external validation of the SMART risk score, the correlation between predicted and observed risk was modest (C-statistic of 0.64; 95% CI 0.63 to 0.65, indicating the model would accurately predict recurrent MACE in 64% of people).[18] The model may overestimate risk in people with highest risk (≥40%) and underestimate risk in people with lower risk.[16,18] Upon internal validation of the REACH registry risk score, predictive ability for recurrent MACE was 67% (C-statistic 0.67; 95% CI 0.66 to 0.68).[17] Predictive ability for CV death was slightly higher (C-statistic 0.75; 95% CI 0.73 to 0.77).[17] However, these models do highlight that risk for recurrent MACE varies significantly depending on the population and type of CV disease. In the population used to externally validate the SMART risk score (n=18,436 patients), overall 10-year risk of recurrent MACE was 17% (interquartile range 11% to 28%), but varied substantially across subgroups.[18] For example, people with coronary artery disease had lower risk (median 14%; interquartile range 10% to 20%) than people with polyvascular disease involving multiple parts of the vacular system (median 35%; interquartile range 23% to 54%).[18]

Secondary *Prevention in Early Cardiovascular Disease*

The 2023 ACC/AHA guidelines highlight the need for development and validation of comprehensive risk scores in patients with chronic coronary artery disease that include patient demographics, medical information, social determinants, and data from test results.[3] In young people, traditional risk factors (like high blood pressure, smoking, hyperlipidemia, diabetes, obesity, physical inactivity, and family history of premature coronary artery disease) continue to be identified as major contributors for CV disease, but studies have identified that other non-traditional risk factors may also elevate risk.[3] The ACC/AHA identifies the following non-traditional risk factors for MACE in young people: HIV, substance use, systemic inflammatory disorders (such as irritable bowel disease, systemic lupus erythematosus, rheumatoid arthritis, gout, psoriatic arthritis, ankylosing spondylitis, and vasculitis), pregnancy-related complications (like gestational diabetes, hypertensive disorders, and intrauterine growth retardation), familial hypercholesterolemia, psychosocial factors (psychological well-being, sleep quality, and social determinants of health), and history of chest radiation.[3]

Observational studies have estimated risk of recurrent events in people with established CV disease before 45 years of age. The AFIJI (Appraisal of Risk Factors in Young Ischemic Patients Justifying Aggressive Intervention) study was a long-term prospective observational study designed to evaluate prognostic risk factors for long-term adverse outcomes in people with coronary artery disease 45 years of age or younger.[5] Participants who had an acute MI or symptomatic obstructive coronary disease (stenosis ≥70%) were enrolled between 1996 and 2017 (n=880).[5] The primary outcome was the first MACE (a composite of death, MI, refractory angina requiring cononary revascularization, and ischemic stroke). Over a 20-year follow-up, 30% of patients experienced recurrent MACE (4.68 events per 100 patient-years).[5] People with the following risk factors had a higher risk for recurrent events: active smoking, uncontrolled diabetes mellitus, and elevated low-density lipoprotein (LDL) cholesterol.[5] People of sub-Saharan African or Asian origin, with multivessel disease, and with initial treatment with coronary artery bypass graft surgery (CABG) also had increased risk of recurrent MACE.[5] Nine percent of patients experienced more than one subsequent recurrent MACE, and death occurrred in 6.3% of people (median time to event of 8.4 years).[5] Another retrospective cohort study (the YOUNG-MI study) evaluated risk of all-cause and CV death in 2097 people who experienced an artherosclerotic MI from 41 to 50 years of age (n=1654) and 40 years of age or younger (n=443).[6] People 40 years of age or younger were more likely to have substance use (primarily marijuana and cocaine) compared to people 41 to 50 years of age, who were more likely to have hypertension, peripheral vascular disease, alcohol use, and a higher ASCVD risk score. Upon discharge after their first MI, very young patients had slightly lower prescribing rates for aspirin, statin, and diuretics.[6] Other pharmacotherapy for CV conditions was similar between groups. Over a median follow-up of 11.2 years, both populations had similar mortality. All-cause mortality was 8.5% in people 40 years of age or younger and 10.7% in people 41-50 years (p=0.17). CV death was 4.2% in both groups (p=1.00).[6] Frequency of non-fatal CV events was not evaluated. A third retrospective study in the Veterans Affairs (VA) health-system also emphasized the role of substance use disorders as a non-traditional risk factor for CV disease. The study included 135,703 patients with premature ASCVD (<55 years of age for men and <65 years of age for women), 1,112,455 people with non-premature ASCVD, and 7,716 patients with extremely premature ASCVD (<40 years of age).[7] Premature ASCVD was identified more commonly in women, non-white populations, people living with obesity or hypercholesterolemia, and people with recreational or illicit substance use.[7] All individual drugs increased odds of premature ASCVD, including tobacco, alcohol, cocaine, amphetamine, cannabis, and other drugs.[7] Risk of premature ASCVD also increased proportionally based on the number of substances used.[7] Similar trends were observed upon comparison of people with extremely premature ASCVD compared to people without premature ASCVD.[7] Data from these types of observational studies are limited by lack of comparator groups, influence of confounding factors, use of historical data, and reliance on claims-based administrative data.

Guideline Recommendations for Established Cardiovascular Disease

In people with established CV disease, the AHA/ACC recommend use of guideline-directed therapy to manage factors that increase risk of recurrent events.[3] Guideline-directed management includes recommendations for lifestyle changes (e.g., diet and exercise), management of comorbid conditions (mental health conditions, substance use, hyperlipidemia, hypertension, diabetes, obesity/overweight), and medication therapy (antiplatelet therapy, beta-blockers, ACE inhibitor/ARB, colchicine, and immunizations).[3] In people with diabetes mellitus, management with a sodium glucose cotransporter-2 (SGLT2) inhibitor or glucagon-like peptide 1 (GLP-1) receptor agonist (RA) with proven CV benefit is recommended. In people living with overweight or obesity, counseling on diet, lifestyle and goals for weight loss is recommended. If pharmacologic therapy is warranted for further weight reduction, a GLP-1 RA may help with further weight reduction, with semaglutide preferred over liraglutide.[3] Sympathomimetic drugs like phentermine or diethylpropion are not recommended because they can increase heart rate and blood pressure.[3] Referral for a bariatric procedure is reasonable in patients with severe obesity who have not met goals for weight management with lifestyle or pharmacologic treatment. In young adults, after optimization of traditional CV risk factors, a comprehensive evaluation and treatment on nontraditional CV risk factors such as chronic inflammation and recreational drug use can be beneficial to reduce the risk of MACE.[3]

The 2017 SIGN guidelines primarily recommend lifestyle changes or surgical interventions to reduce cardiovascular risk associated with overweight and obesity in people at risk for CV disease. They recommend that individuals should aim to reduce weight by at least 3 kg, and to maintain weight reduction.[4] No

recommendations were included for specific medications to manage obesity, but these guidelines were published prior to studies evaluating cardiovascular outcomes in this population.

NICE guidelines for treatment of MI or peripheral arterial disease recommend offering all people living with overweight or obesity advice and support to achieve and maintain a healthy weight for secondary prevention of CV disease.[8,9] Recommendations for weight management encompass several interventions, including lifestyle, behavioral, physical activity, dietary, pharmacological, and surgical interventions. Drug treatment (including orlistat, liraglutide, or semaglutide) should be considered for people who have not reached their target weight loss or have stopped loosing weight after dietary, physical activity and behavioral changes.[19] A higher level of intervention is generally recommended for people with weight-related comorbidities such as CV disease, hypertension, dyslipidemia, sleep apnea, osteoarthritis, and type 2 diabetes mellitus.[19] Semaglutide is specifically recommended for all patients with a BMI of at least 35 mg/m^2 in the absence of comorbid conditions or other risk factors for CV disease.[19] Lower BMI thresholds may be appropriate for some people based on other risk factors.[19]

Semaglutide in people with Early Cardiovascular Disease

Because the SELECT trial excluded people less than 45 years of age, there are no data from clinical trials that have evaluated CV benefit for semaglutide in this age group.[1] Additionally, trials evaluating CV effects of semaglutide in people with diabetes mellitus and established CV disease have not included people younger than 45 years of age.[20,21] In people with diabetes mellitus, injectable semaglutide was studied people over 50 years of age and oral semaglutide was studied in people over 60 years of age.[20,21] In people with diabetes melltus, injectable semaglutide demonstrated differences in CV outcomes compared to placebo after 2 years, and oral semaglutide was non-inferior to placebo over 16 months.[20,21]

However, while prevalence of CV disease increases with age, data from observational studies indicate that people with early CV disease may have similar risk for recurrent events as people with CV disease who are over 45 years of age. A prior CV event is a major predictor for recurrent events, and most guidelines categorize people with established CV disease to be at high risk for recurrent MACE (>10% risk over 10 years). Data from observational studies suggests that risk may vary significantly depending on individual risk factors, comorbid conditions, and type of CV event. Guidelines consistently recommend weight management (including lifestyle changes and drug therapy) in people with CV disease who are living with overweight or obesity.

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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 and nonalcoholic steatohepatitis (NASH, also called metabolic dysfunction-associated steatohepatitis [MASH]).

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

Table 3. Evidence-Supported Indications

Drug	Indications
Liraglutide	• Biopsy-confirmed non-alcoholic steatohepatitis (NASH) in adults 18 years and older
Semaglutide	• Established cardiovascular disease (e.g., history of myocardial infarction, stroke, or symptomatic peripheral arterial disease) • Biopsy-confirmed non-alcoholic steatohepatitis (NASH) in adults 18 years and older

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is this a request for continuation of therapy after an initial approval by FFS?	**Yes**: Go to renewal criteria	**No:** Go to #3

Approval Criteria		
3. Does the patient have a BMI corresponding to one of the following: 1) ≥30 kg/m^2 or 2) ≥27 kg/m^2 and comorbid conditions [e.g., diabetes mellitus, hypertension, dyslipidemia, fatty liver disease, or cardiovascular disease] or ~~1)~~3) a BMI at the 95th percentile or greater for age and sex (Table 2 above)?	**Yes:** Go to #4 Record baseline BMI	**No:** Deny; medical appropriateness
4. Will the patient be engaged in a weight management lifestyle modification program in addition to pharmacotherapy? See clinical notes below	**Yes:** Go to #5	**No:** Deny; medical appropriateness. All drugs approved for weight loss are indicated as an adjunct to diet and exercise.
~~3.~~5. Is the requested medication for an FDA-approved age (Table 1) in a patient less than 21 years of age ~~and 6 years of age or older~~?	**Yes:** Go to #~~3~~6	**No:** Go to #1~~2~~
~~4.~~6. Is the request for setmelanotide?	**Yes**: Go to #~~6~~7	**No:** Go to #~~8~~9
~~5.~~7. 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~~8	**No:** Deny; medical appropriateness.
~~6.~~8. Does the patient have a history of depression and/or suicidal ideation?	**Yes**: Deny; medical appropriateness.	**No:** Approve for up to 6 months.

Approval Criteria		
~~7. Does the patient have a BMI corresponding to 30 kg/m^2 or ≥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~~
~~13.~~9. Does the patient have comorbidities (e.g., hypertension, dyslipidemia, diabetes, fatty liver disease, depression, or sleep apnea)?	**Yes:** ~~Go to #11~~Approve for 6 months	**No:** Go to #10
~~14.~~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:** Approve for 6 months. ~~Go to #11~~	**No:** Deny; medical appropriateness. Lifestyle modifications are recommended by guidelines.
~~15. 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.~~
11. Is the request for a drug FDA-approved or compendia supported for the requested condition as defined in Table 3?~~Is the request for a weight management drug with an FDA-approved indication for secondary cardiovascular prevention?~~	**Yes:** Go to #~~13~~12	**No:** Pass to RPh. Deny; drugs are not covered by OHP for adults when indicated for weight loss.
~~19. Does the patient have established cardiovascular disease (e.g., history of myocardial infarction, stroke, or symptomatic peripheral arterial disease)?~~	~~**Yes**: Go to #13~~	~~**No:** Deny; drugs are not covered by OHP for adults when indicated for weight loss.~~

Approval Criteria		
~~23. Is the request for continuation of therapy previously approved by FFS?~~	~~**Yes:** Go to Renewal Criteria~~	~~**No:** Go to #14~~
12. 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 #~~15~~13	**No:** Deny; medical appropriateness
~~27.~~13. Is there documentation of a type 2 diabetes diagnosis?	**Yes:** Go to #15	**No:** Go to #14
~~28.~~14. Has the patient been screened for diabetes within the past year and do screening 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 screening and if positive recommend a GLP-1 RA indicated for glucose lowering (see GLP-1 RA/GIP RA PA criteria)
~~29. 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.~~
15. Is the request for semaglutide?	**Yes:** Go to #16	**No:** Approve for up to 6 months
~~35.~~16. 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 #17~~20~~
~~36.~~17. Will the patient try semaglutide (Ozempic) for at least ~~6~~ 4 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) or NASH?	**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
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-	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

sweetened beverages (SSBs)	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	

P&T/DUR Review: 6/24 (KS)
Implementation: 7/1/24

Glucagon-like Peptide-1 (GLP-1) Receptor Agonists and Glucose Dependent Insulinotropic Polypeptide (GIP) Receptor Agonist

Goal(s):

- Promote cost-effective and safe step-therapy for management of type 2 diabetes mellitus (T2DM).

Length of Authorization:

- Up to 12 months

Requires PA:
- All non-preferred GLP-1 receptor agonists and GLP-1 receptor + GIP receptor agonists. Preferred products do not require PA when prescribed as second-line therapy in conjunction with metformin.

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/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code	
2. Does the patient have a diagnosis of Type 2 diabetes mellitus?	**Yes:** Go to #3	**No:** Pass to RPh. Deny; medical appropriateness. For requests for non-alcoholic or metabolic dysfunction-associated steatohepatitis (NASH/MASH), see weight management PA criteria.
3. Will the prescriber consider a change to a preferred product? Message: • Preferred products are evidence-based reviewed for comparative effectiveness and safety by the Oregon Pharmacy and Therapeutics (P&T) Committee.	**Yes:** Inform prescriber of covered alternatives in class	**No:** Go to #4
4. Has the patient tried and failed to meet hemoglobin A1C goals with metformin or have contraindications to metformin? (document contraindication, if any)	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness. Recommend trial of metformin. See below for metformin titration schedule.

Initiating Metformin

1.	Begin with low-dose metformin (500 mg) taken once or twice per day with meals (breakfast and/or dinner) or 850 mg once per day.
2.	After 5-7 days, if gastrointestinal side effects have not occurred, advance dose to 850 mg, or two 500 mg tablets, twice per day (medication to be taken before breakfast and/or dinner).
3.	If gastrointestinal side effects appear with increasing doses, decrease to previous lower dose and try to advance the dose at a later time.
4.	The maximum effective dose can be up to 1,000 mg twice per day. Modestly greater effectiveness has been observed with doses up to about 2,500 mg/day. Gastrointestinal side effects may limit the dose that can be used.

Nathan, et al. Medical management of hyperglycemia in Type 2 Diabetes: a consensus algorithm for the initiation and adjustment of therapy. *Diabetes Care*. 2008; 31;1-11.

P&T Review: *10/22 (KS), 8/20 (KS), 6/20), 3/19, 7/18, 9/17; 1/17; 11/16; 9/16; 9/15; 1/15; 9/14; 9/13; 4/12; 3/11*
Implementation: *1/1/23; 9/1/20; 5/1/19; 8/15/18; 4/1/17; 2/15; 1/14*