Pharmacy Policy Bulletin

Title:	Weight Loss Agents
Policy #:	Rx.01.94

Application of pharmacy policy is determined by benefits and contracts. Benefits may vary based on product line, group, or contract. Some medications may be subject to precertification, age, quantity, or formulary restrictions (ie limits on non-preferred drugs). Individual member benefits must be verified.

This pharmacy policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety, or FDA approval may have changed. This Pharmacy Policy will be regularly updated as scientific and medical literature becomes available. This information may include new FDA-approved indications, withdrawals, or other FDA alerts. This type of information is relevant not only when considering whether this policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Intent:

The intent of this policy is to communicate the medical necessity criteria for weight loss agents as provided under the member's prescription drug benefit.

Description:

Weight loss agents are a standard exclusion for some benefits. Prior authorization review for medical necessity is required when stated in the member's prescription drug benefit contract that includes coverage for weight loss products.

Obesity is associated with significant mortality and a risk factor for many diseases including type 2 diabetes, hypertension, dyslipidemia, and cardiovascular disease, obstructive sleep apnea. Obesity is categorized by body mass index:

Category	BMI
Underweight	<18.5 kg/m^2
Normal weight	18.5-24.9 kg/m^2
Overweight	25-29.9 kg/m^2
Obesity	30 kg/m^2 or greater
Severe obesity	40 kg/m^2 or greater (35 kg/m^2 or greater in presences of comorbidities)

The goal of therapy is to prevent, treat, or reverse complications associated with obesity. Comprehensive lifestyle modifications, including diet, exercise, and behavioral modifications are the cornerstone of weight loss plans. Drug therapy may be considered as an adjunct to lifestyle modifications. Per Endocrine Society Clinical Guideline, to promote long-term weight maintenance, the use of approved weight loss drugs is suggested over no pharmacotherapy to ameliorate comorbidities and amplify adherence to behavior changes in those with BMI ≥ 30 or BMI ≥ 27 with at least one comorbidity. Benzphetamine, diethylpropion [ER], phendimetrazine [ER], phentermine are sympathomimetic amines similar to amphetamines. The exact mechanism of action for weight loss has not been established but may include appetite suppression and other central nervous system actions or metabolic effects.

Liraglutide and Semaglutide are a glucagon-like peptide 1 (GLP-1) agonists. GLP-1 is a physiological regulator of appetite and calorie intake, and the GLP-1 receptor is present in several areas of the brain involved in appetite regulation. Liraglutide and Semaglutide lowers body weight through decreased calorie intake.

Naltrexone/bupropion have effects on two separate areas of the brain involved in the regulation of food intake: the hypothalamus (appetite regulatory center) and the mesolimbic dopamine circuit (reward system). The exact neurochemical effects leading to weight loss are not fully understood.

Orlistat is a reversible inhibitor of gastrointestinal lipases. It exerts its therapeutic activity in the lumen of the stomach and small intestine by forming a covalent bond with the active serine residue site of gastric and pancreatic lipases. The inactivated enzymes are thus unavailable to hydrolyze dietary fat in the form of triglycerides into absorbable free fatty acids and monoglycerides. As undigested triglycerides are not absorbed, the resulting caloric deficit may have a positive effect on weight control.

Topiramate's mechanism of action for weight loss is unknown. It may be related to appetite suppression and satiety enhancement induced by a combination of pharmacologic effects including augmenting the activity of the neurotransmitter gamma-aminobutyrate, modulation of voltage-gated ion channels, inhibition of AMPA/kainite excitatory glutamate receptors, or inhibition of carbonic anhydrase.

Amphetamine's mechanism of action for weight loss has not been established. However, that the action of such drugs in treating obesity is primarily one of appetite suppression. Other central nervous system actions or metabolic effects may be involved.

Benzphetamine, diethylpropion, phendimetrazine, phentermine (Adipex-P®, Lomaira®) are indicated in the management of exogenous obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction in patients with an initial body mass index (BMI) of 30 kg/m2 or higher who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone. Phendimetrazine and phentermine (Adipex-P®, Lomaira®) are also indicated with an initial BMI greater than or equal to 27 kg/m2 in the presence of other risk factors (e.g., controlled hypertension, diabetes, hyperlipidemia) who have not responded to appropriate weight reducing regimen (diet and/or exercise) alone. For those with uncontrolled hypertension, the use of sympathomimetic agents is generally not recommended.

Orlistat (Xenical®) is indicated for obesity management including weight loss and weight maintenance when used in conjunction with a reduced-calorie diet and to reduce the risk for weight regain after prior weight loss. Orlistat is indicated for obese patients aged 12 years or older with an initial body mass index (BMI) ≥30 kg/m2 or ≥27 kg/m2 in the presence of other risk factors (e.g., hypertension, diabetes, dyslipidemia). *For member's 12 to 17 years of age, use the Cole criteria for the corresponding BMI for member's age and sex.

Phentermine/ topiramate (Qsymia®), naltrexone/ bupropion (Contrave®)are indicated as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adult patients with an initial BMI ≥30 kg/m2 or ≥27 kg/m2 in the presence of at least one weight-related comorbid conditions (e.g., hypertension, diabetes, dyslipidemia).

Liraglutide (Saxenda®), and semaglutide (Wegovy®) are indicated as an adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adults with initial body mass index (BMI) ≥30 kg/m2 or ≥27 kg/m2 in the presence of at least one weight-related comorbid conditions (e.g., hypertension, diabetes, dyslipidemia).

Liraglutide (Saxenda®) is also indicated in pediatric patients aged 12 years and older with body weight above 60 kg and initial BMI corresponding to 30 kg/m2 or greater in adults (obese) by international cut-offs (Cole Criteria).

Semaglutide (Wegovy®) is also indicated in pediatric patients aged 12 years and older with an initial BMI at the 95th percentile or greater for age and sex (obesity).

Amphetamine (Evekeo®) is indicated as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction for patients refractory to alternative therapy, e.g., repeated diets, group programs, and other drugs. The limited usefulness of amphetamines be weighed against possible risks inherent in use of the drug.

International Obesity Task Force BMI Cut-offs for Obesity by Sex and Age for Pediatric Patients Aged 12 Years and Older (Cole Criteria)

Age (years)	Body Mass Index $30kg/m^2$	
	Males	Females
12	26.02	26.67
12.5	26.43	27.24
13	26.84	27.76
13.5	27.25	28.2
14	27.63	28.57

14.5	27.98	28.87
15	28.3	29.11
15.5	28.6	29.29
16	28.88	29.43
16.5	29.14	29.56
17	29.41	29.69
17.5	29.7	29.84

Policy:

Short-term Weight Reduction

INITIAL CRITERIA: Amphetamine (Evekeo®), Diethylpropion, diethylpropion ER, benzphetamine, phendimetrazine tablet, phendimetrazine ER capsule, or phentermine (Adipex-P, Lomaira) is approved when ALL of the following are met:

1. Submission of documentation (e.g., chart note) confirming one of the following:
    a. Diagnosis of obesity defined as BMI ≥ 30 kg/m^2*; or
    b. Both of the following:
        i. BMI ≥ 27 kg/m2; and
        ii. ii. Member has one or more comorbidities (e.g., hypertension, coronary artery disease, type 2 diabetes mellitus, dyslipidemia, or obstructive sleep apnea); and
2. One of the following:
    a. For diethylpropion, diethylpropion ER, phendimetrazine ER capsule, phentermine [Adipex-P, Lomaira] only, member is 17 years of age or older; or
    b. For phendimetrazine, benzphetamine only, member is 18 years of age or older; and
3. Drug will be used short-term (a few weeks) as adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
4. For brand Adiphex-P and brand Lomaira requests only, inadequate response or inability to tolerate generic phentermine; and
5. For brand Evekeo® only, inadequate response or inability to tolerate generic amphetamine

Initial authorization duration: 4 months

REAUTHORIZATION CRITERIA: Amphetamine (Evekeo®), Diethylpropion, diethylpropion ER, benzphetamine, phendimetrazine tablet, phendimetrazine ER capsule, or phentermine (Adipex-P, Lomaira) is re-approved when ALL of the following are met:

1. Cumulative therapy does not exceed 4 months in 365 days; and
2. No documentation of treatment with requested drug within the past 4 months

Reauthorization duration: 4 months

Chronic Weight Management

INITIAL CRITERIA Semaglutide (Wegovy) is approved when ALL of the following are met:

1. One of the following:
    a. Member is 18 years of age or older with submission of documentation (e.g., chart note) confirming ONE of the following:
        i. Diagnosis of obesity defined as BMI ≥ 30 kg/m^2; or
        ii. Both of the following:
            1. BMI ≥ 27 kg/m2; and
            2. Member has one or more comorbidities (e.g., hypertension, coronary artery disease, type 2 diabetes mellitus, dyslipidemia, or obstructive sleep apnea); and
    b. Member is 12 to 17 years of age with submission of documentation (e.g., chart note) confirming an initial BMI at the 95th percentile or greater for age and sex (obesity); and
2. Drug will be used as adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
3. No concurrent use of any other GLP-1 receptor agonist (e.g., Ozempic, Rybelsus, Trulicity, Victoza)

Initial authorization duration: 7 months

REAUTHORIZATION CRITERIA Semaglutide (Wegovy) is re-approved when ALL of the following are met:

1. Drug will be used as adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
2. Submission of documentation (e.g., chart note) confirming weight loss of greater than or equal to 5% from baseline body weight; and
3. No concurrent use of any other GLP-1 receptor agonist (e.g., Ozempic, Rybelsus, Trulicity, Victoza)

Reauthorization duration: 6 months

INITIAL CRITERIA Liraglutide (Saxenda) is approved when ALL of the following are met:

1. One of the following:
    a. Member is 18 years of age or older with submission of documentation (e.g., chart note) confirming one of the following:
        i. Diagnosis of obesity defined as BMI ≥ 30 kg/m^2; or
        ii. Both of the following:
            1. BMI ≥ 27 kg/m2; and
            2. Member has one or more comorbidities (e.g., hypertension, coronary artery disease, type 2 diabetes mellitus, dyslipidemia, or obstructive sleep apnea); or
    b. Member is 12 to 17 years of age with submission of documentation (e.g., chart note) confirming both of the following:
        i. Body weight above 60kg; and
        ii. BMI corresponding to 30 kg/m2 for adults (obese) by international cut-offs (Cole Criteria)*; and
2. Drug will be used as adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
3. No concurrent use of any other GLP-1 receptor agonist (e.g., Ozempic, Trulicity, Victoza)

Initial authorization duration: 5 months

REAUTHORIZATION CRITERIA Liraglutide (Saxenda) is re-approved when ALL of the following are met:

1. Drug will be used as adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
2. One of the following:
    a. For members 18 years of age or older, submission of documentation (e.g., chart note) confirming weight loss of greater than or equal to 4% from baseline body weight; or
    b. For members 12 to 17 years of age, submission of documentation (e.g., chart note) confirming weight loss greater than or equal to 1% from baseline body weight; and
3. No concurrent use of any other GLP-1 receptor agonist (e.g., Ozempic, Trulicity, Victoza)

Reauthorization duration: 6 months

INITIAL CRITERIA Phentermine/topiramate (Qsymia), naltrexone/bupropion (Contrave); orlistat (Xenical) is approved when all of the following are met:

1. Submission of documentation (e.g., chart note) confirming one of the following:
    a. Diagnosis of obesity defined as BMI ≥ 30 kg/m^2; or
    b. Both of the following:
        i. BMI ≥ 27 kg/m2; and
        ii. Member has one or more comorbidities (e.g., hypertension, coronary artery disease, type 2 diabetes mellitus, dyslipidemia or obstructive sleep apnea); and
2. One of the following:
    a. For phentermine/topiramate (Qsymia) and naltrexone/bupropion (Contrave) only, member is 18 years of age or older; or
    b. For orlistat (Xenical) only, member is 12 years of age or older; and

3. Drug will be used as adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program)

Initial authorization duration: 6 months

REAUTHORIZATION CRITERIA phentermine/topiramate (Qsymia), naltrexone/bupropion (Contrave), orlistat (Xenical) is re-approved when ALL of the following are met:

1. Drug will be used as adjunct to lifestyle modification (e.g., dietary or caloric restriction, exercise, behavioral support, community-based program); and
2. Submission of documentation (e.g., chart note) confirming weight loss of greater than or equal to 5% from baseline body weight

Reauthorization duration: 6 months

NOTES: *For member's 12 to 17 years of age, use the Cole criteria for the corresponding BMI for member's age and sex. International Obesity Task Force BMI Cut-offs for Obesity by Sex and Age for Pediatric Patients Aged 12 Years and Older (Cole Criteria)

Age (years)	Body Mass Index 30kg/m^2	
	Males	Females
12	26.02	26.67
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16	28.88	29.43
16.5	29.14	29.56
17	29.41	29.69
17.5	29.7	29.84

Black Box Warning as shown in the drug Prescribing Information:
Contrave ER® (naltrexone/bupropion)

SUICIDAL THOUGHTS AND BEHAVIORS; AND NEUROPSYCHIATRIC REACTIONS

SUICIDALITY AND ANTIDEPRESSANT DRUGS

Naltrexone/ bupropion is not approved for use in the treatment of major depressive disorder or other psychiatric disorders. Naltrexone/ buprenorphine contains bupropion, the same active ingredient as some other antidepressant medications (including, but not limited to, WELLBUTRIN®, WELLBUTRIN SR®, WELLBUTRIN XL® and APLENZIN®). Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term trials. These trials did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in subjects over age 24; there was a reduction in risk with antidepressant use in subjects aged 65 and older. In patients of all ages who are started on naltrexone/ buprenorphine, monitor closely for worsening, and for the emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber. Naltrexone/ buprenorphine is not approved for use in pediatric patients

NEUROPSYCHIATRIC REACTIONS IN PATIENTS TAKING BUPROPION FOR SMOKING CESSATION

Serious neuropsychiatric reactions have occurred in patients taking bupropion for smoking cessation. The majority of these reactions occurred during bupropion treatment, but some occurred in the context of discontinuing treatment. In many cases, a causal relationship to bupropion treatment is not certain, because depressed mood may be a symptom of nicotine withdrawal. However, some of the cases occurred in patients taking bupropion who continued to smoke.

Although naltrexone/ bupropion is not approved for smoking cessation, observe all patients for neuropsychiatric reactions. Instruct the patient to contact a healthcare provider if such reactions occur.

Saxenda® (liraglutide), Wegovy® (Semaglutide)

RISK OF THYROID C-CELL TUMORS

Both Liraglutide and Semaglutide cause~~s~~ dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether these drugs causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced or semaglutide-induced rodent thyroid C-cell tumors has not been determined.

Liraglutide and Semaglutide are~~is~~ contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk of MTC with use of either liraglutide or semaglutide and inform them of symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with liraglutide or semaglutide.

Evekeo® (amphetamine sulfate)

Amphetamines have a high potential for abuse. administration of amphetamines for prolonged periods of time may lead to drug dependence and must be avoided. particular attention should be paid to the possibility of subjects obtaining amphetamines for non-therapeutic use or distribution to others, and the drugs should be prescribed or dispensed sparingly.

Misuse of amphetamine may cause sudden death and serious cardiovascular adverse events.

Guidelines:

Refer to the specific manufacturer's prescribing information for administration and dosage details and any applicable Black Box warnings.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable benefit contract, the applicable drug(s) identified in this policy is (are) covered under the prescription drug benefits of the Company’s products when the medical necessity criteria listed in this pharmacy policy are met. Any services that are experimental/investigational or cosmetic are benefit contract exclusions for all products of the Company.

References:

Adipex-P® (phentermine) [package insert]. Horsham, PA. Teva Select Brands. September 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=f5b2f9d8-2226-476e-9caf-9d41e6891c46&type=display. Accessed April 20, 2023.

Benzphetamine [package insert]. East Brunswick, NJ. Heritage Pharmaceuticals Inc. December 2019. Available at https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=3fd6b3a8-b17b-4b98-ad03-a8af7b6f3368&type=display. Accessed April 20, 2023

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Contrave® (naltrexone/ bupropion) [package insert]. Deerfield, IL. Takeda Pharmaceuticals America, Inc. April 2019. Available at: https://contrave.com/content/pdf/Contrave_PI.pdf. Accessed April 20, 2023.

Diethylpropion IR/ CR [package insert]. Parsippany, NJ. Actavis Pharma, Inc. October 2018. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=a750a1ef-8f3e-4870-97eb-3697aaca1818&type=display. Accessed April 20, 2023.

Evekeo® (amphetamine salts) [package insert]. Atlanta, GA: Arbor Pharmaceuticals, LLC. April 2019. Available at: https://www.evekeo.com/pdfs/evekeo-pi.pdf?v=1680099069680. Accessed April 20, 2023.

Lomaira® (phentermine) [package insert]. Newtown, PA. KVK-Tech Inc. December 2018. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=cde9fb09-e5af-434d-8874-e4f9f974d893&type=display. Accessed April 20, 2023

Apovian, Caroline M, et, al. Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab, February 2015. Accessed April 20 2023.

Qsymia® (phentermine/ topiramate) [package insert]. Mountain View, CA. Vivus, Inc. June 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=40dd5602-53da-45ac-bb4b-15789aba40f9&type=display#section-12.1. Accessed April 20, 2023.

Saxenda® (liraglutide) [package insert]. Plainsboro, NJ. Novo Nordisk. June 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=3946d389-0926-4f77-a708-0acb8153b143&type=display.%20 Accessed April 20, 2023.

Wegovy® (semaglutide) [package insert] Novo Nordisk. December 2022. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=ee06186f-2aa3-4990-a760-757579d8f77b&type=display Accessed April 20, 2023.

Xenical® (orlistat) [package insert]. South San Francisco, CA. Genentech USA, Inc. December 2018. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=5bbdc95b-82a1-4ba5-8185-6504ff68cc06&type=display. Accessed April 20, 2023.

Applicable Drugs:

Inclusion of a drug in this table does not imply coverage. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

Brand Name	Generic Name
Xenical®	Orlistat
Didrex® and Regimex®	Benzphetamine
	Diethylpropion [ER]
	Phendimetrazine
Adipex-P®, Lomaira®	Phentermine
Qsymia®	Phentermine/topiramate
Contrave ER®	Naltrexone/bupropion hcl
Saxenda®	Liraglutide
Wegovy®	Semaglutide
Evekeo®	Amphetamine

Cross References:

Off-Label Use Policy Rx.01.33

Policy Version Number:	17.00
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