

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 most 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. Obesity is categorized by body mass index:

Category	BMI
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.

Benzphetamine, diethylpropion, phendimetrazine, 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 is a glucagon-like peptide 1 (GLP-1) agonist. 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 lowers body weight through decreased calorie intake.

Lorcaserin is believed to decrease food consumption and promote satiety by selectively activating 5-HT_{2C} receptors on anorexigenic pro-opiomelanocortin neurons located in the hypothalamus. The exact mechanism of action is not known.

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.

Benzphetamine (Didrex®, Regimex®), diethylpropion, phendimetrazine, phentermine (Adipex-P®, Lomaira®, Suprenza®) 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®, Suprenza®) 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.

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 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).

Phentermine/ topiramate (Qsymia®), lorcaserin (Belviq [XR] ®), liraglutide (Saxenda®), 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).

▸ **Policy:**

A weight loss agent is approved when there is documentation of morbid obesity defined by ANY of the following:

1. Body Mass Index (BMI) greater than 40 kg/m²; or
2. Body weight 45 kilograms (100 pounds) or more above Ideal Body Weight (IBW); or
3. Body weight 100 percent or more above IBW; or
4. BMI between 35 and 40 kg/m² in conjunction with one or more comorbidities related to obesity (e.g. hypertension, coronary artery disease, type 2 diabetes mellitus, or obstructive sleep apnea)

Authorization duration: 2 years

**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)

RISK OF THYROID C-CELL TUMORS

Liraglutide causes 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 liraglutide

causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors has not been determined.

Liraglutide 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 liraglutide 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.

▸ **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. March 2017. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=f5b2f9d8-2226-476e-9caf-9d41e6891c46&type=display>. Accessed February 18, 2019.

Belviq® (lacoserin) [package insert]. Woodcliff Lake, NJ. Eisai Inc. May 2017. Available at: https://www.belviq.com/-/media/Files/BelviqConsolidation/PDF/Belviq_Prescribing_information-pdf.PDF?la=en. Accessed February 18, 2019

Belviq XR® (lacoserin XR) [package insert]. Woodcliff Lake, NJ. Eisai Inc. May 2017. Available at: https://www.belviq.com/-/media/Files/BelviqConsolidation/PDF/Belviq_Prescribing_information-pdf.PDF?la=en. Accessed February 18, 2019.

Bray GA. Obesity in adults: overview of management. UpToDate. October 2018. Available at: https://www.uptodate.com/contents/obesity-in-adults-overview-of-management?source=search_result&search=weight%20loss&selectedTitle=2~150. Accessed February 18, 2019.

Contrave® (naltrexone/ bupropion) [package insert]. Deerfield, IL. Takeda Pharmaceuticals America, Inc. August 2018. Available at: https://contrave.com/content/pdf/Contrave_PI.pdf Accessed February 18, 2019.

Didrex® (benzphetamine) [package insert]. New York, NY. Pharmacia & Upjohn Company. December 2016. Available at: <http://labeling.pfizer.com/ShowLabeling.aspx?id=565> Accessed February 18, 2019.

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 February 18, 2019.

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 February 18, 2019.

Qsymia® (phentermine/ topiramate) [package insert]. Mountain View, CA. Vivus, Inc. November 2018. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=40dd5602-53da-45ac-bb4b-15789aba40f9&type=display#section-12.1>. Accessed February 18, 2019.

Regimex® (benzphetamine) [package insert]. Ridgeland, MS. WraSer Pharmaceuticals. March 2013. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=1a5d7233-4453-42a5-8144-a4276db39660&type=display>. Accessed February 18, 2019.

Saxenda® (liraglutide) [package insert]. Plainsboro, NJ. Novo Nordisk. October 2018. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=3946d389-0926-4f77-a708-0acb8153b143&type=display>. Accessed February 18, 2019.

Suprenza® (phentermine) [package insert]. Cranford, NJ. Akrimax Pharmaceuticals, LLC. June 2013. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=b961e6cc-4956-405f-9e53-b55604be23f6&type=display>. Accessed February 18, 2019.

Xenical® (orlistat) [package insert]. South San Francisco, CA. Genentech USA, Inc. August 2016. Available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=5bbdc95b-82a1-4ba5-8185-6504ff68cc06&type=display>. Accessed February 18, 2019.

Applicable Drugs:

i 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®, Suprenza ODT®	Phentermine
Qsymia®	Phentermine/topiramate
Belviq [XR]®	Lorcaserin [XR]
Contrave ER®	Naltrexone/bupropion hcl
Saxenda®	Liraglutide

Cross References:

N/A

Policy Version Number:	11.00
P&T Approval Date:	January 10, 2019
Policy Effective Date:	April 01, 2019
Next Required Review Date:	January 10, 2020

The Policy Bulletins on this web site were developed to assist the Company in administering the provisions of the respective benefit programs, and do not constitute a contract. If you have coverage through the Company, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. Company does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of the Company. If you have a specific medical condition, please consult with your doctor. The Company reserves the right at any time to change or update its Policy Bulletins.