MEDICATION COVERAGE POLICY

PHARMACY AND THERAPEUTICS ADVISORY COMMITTEE

Health Plan of San Joaquin

POLICY:	Weight Loss	**P&T DATE:**	9/14/2021
THERAPEUTIC CLASS:	Gastrointestinal Disorders	**REVIEW HISTORY:** (MONTH/YEAR)	9/20, 9/19, 9/18, 5/17, 5/16
LOB AFFECTED:	Medi-Cal		

This policy has been developed through review of medical literature, consideration of medical necessity, generally accepted medical practice standards, and approved by the HPSJ Pharmacy and Therapeutic Advisory Committee.

OVERVIEW

Diet, exercise, and behavioral modification are all recommended as first line of obesity management prior to pharmacotherapy and bariatric surgery interventions. The Endocrine Society developed a clinical practice guideline in hopes of re-iterating this concept to streamline an approach towards achieving long-term weight maintenance. With the addition of approved weight loss medications to the treatment regimen, amplification of adherence to proposed behavior changes and possibly improved ability to engage in physical activity can occur. Candidates for weight loss medications would be those who have a history of unsuccessfully losing and maintaining their weight. Health Plan of San Joaquin will cover Bariatric Surgery if the patient meets the medical necessity requirements per the Milliman Care Guidelines. The purpose of this coverage policy will be to examine currently FDA approved agents for weight management and their coverage criteria.

Table 1: FDA-Approved Weight Loss Agents *(Current as of 8/2020)*

Therapeutic Class	*Generic (Brand)*	*Strengths*	*Formulary Status*	*Avg Cost Per RX*	*Notes*
Lipase Inhibitor	Orlistat (Alli-OTC, Xenical)	Alli: 60 mg Capsules	PA	$43.98	[1] BMI of ≥ 27 with 2 or more comorbidities OR [2] BMI > 30
		120 mg Capsules		$623.90	
Serotonin 5-HT_{2C} Receptor Agonist	Lorcaserin Hcl (Belviq)	10 mg Tablets	NF	--	
		20 mg XR Tablets		--	
Sympathomimetics	Benzphetamine Hcl (Regimex)	25 mg Tablets	NF	--	
		50 mg Tablets		--	
		Regimex 25 mg Tablets		--	
	Diethylpropion Hcl (Tenuate)	25 mg Tablets	NF	--	
		75 mg ER Tablets		--	
	Phendimetrazine Tartrate (Bontril)	35 mg Tablets	NF	--	
		105 mg Capsules		--	
	Phentermine (Adipex-P, Lomaira)	8 mg Tablets	NF	--	
		37.5 mg Tablets	F	$2.63	
		15 mg Capsules		$4.12	
		30 mg Capsules		$4.56	
		37.5 mg Capsules		$3.39	
		Adipex-P 37.5 mg Tablets	NF	--	
		Adipex-P 37.5 mg Capsules		--	
GLP-1 Agonist	Liraglutide (Saxenda)	18 mg/3 mL Pen	NF	$1,033.26	
Opioid Antagonist-Dopamine/Norepinephrine Reuptake Inhibitor	Bupropion/ Naltrexone (Contrave)	8/90 mg Tablets	NF	$283.55	

Combination	Phentermine/ Topiramate (Qsymia)	Qsymia 3.75/23 mg Tablets	NF	--	
		Qsymia Tablets 7.5/46 mg		--	
		Qsymia Tablets 11.25/69 mg		--	
		Qsymia Tablets 15/92 mg		--	

ODT = Orally disintegrating tablet; F = Formulary, ST = Step therapy, PA = Prior Authorization required.

Clinical Justification:

Body mass index (BMI), waist circumference, and overall medical risk are part of routine patient weight loss assessment. BMI can be estimated using the following equation: BMI = [weight (in pounds) X 703] / height (inches) squared. [2]

Waist circumference evaluations are used to assess the risk associated with obesity or overweight. Although waist circumference evaluation is of little use in individuals with BMI ≥ 35 kg/m^2, it is of particular value in individuals who fall into BMI classification of normal to overweight. Waist circumference > 40 inches in men, and > 35 inches in women are higher risk of diabetes, dyslipidemia, hypertension, and cardiovascular disease.

Table 6. Classification of Overweight and Obesity by BMI and Waist Circumference (31 [EL 4; NE])

Classification	BMI		Waist	
	BMI (kg/m^2)	Comorbidity Risk	Waist Circumference and Comorbidity Risk	
			Men ≤40 in (102 cm) Women ≤35 in (88 cm)	Men >40 in (102 cm) Women >35 in (88 cm)
Underweight	<18.5	Low but other problems		
Normal weight	18.5–24.9	Average		
Overweight	25–29.9	Increased	Increased	High
Obese class I	30–34.9	Moderate	High	Very high
Obese class II	35–39.9	Severe	Very high	Very high
Obese class III	≥40	Very severe	Extremely high	Extremely high

Abbreviations: BMI = body mass index; in = inches.

AACE/ACE Obesity CPG, Endocr Pract. 2016;22(Suppl 3)

Risk factors for obesity-related disorders include:

Risk Factors

- Cigarette smoking.
- Hypertension (systolic blood pressure of ≥140 mm Hg or diastolic blood pressure ≥ 90 mm Hg) or current use of antihypertensive agents.
- High-risk low-density lipoprotein (LDL) cholesterol (serum concentration ≥ 160 mg/dL). A borderline high-risk LDL-cholesterol (130 to 159 mg/dL) plus two or more other risk factors also confers high risk.
- Low high-density lipoprotein (HDL) cholesterol (serum concentration < 35 mg/dL).
- Impaired fasting glucose (IFG) (fasting plasma glucose between 110 and 125 mg/dL). IFG is considered by many authorities to be an independent risk factor for cardiovascular (macrovascular) disease, thus justifying its inclusion among risk factors contributing to high absolute risk. IFG is well established as a risk factor for type 2 diabetes.
- Family history of premature CHD (myocardial infarction or sudden death experienced by the father or other male first-degree relative at or before 55 years of age, or experienced by the mother or other female first-degree relative at or before 65 years of age).
- Age ≥ 45 years for men or age ≥ 55 years for women (or postmenopausal).

A Guide to Selecting Treatment

	BMI category				
Treatment	**25–26.9**	**27–29.9**	**30-34.9**	**35–39.9**	**≥ 40**
Diet, physical activity, and behavior therapy	With comorbidities	With comorbidities	+	+	+
Pharmacotherapy		With comorbidities	+	+	+
Surgery				With comorbidities	

- Prevention of weight gain with lifestyle therapy is indicated in any patient with a BMI ≥ 25 kg/m^2, even without comorbidities, while weight loss is not necessarily recommended for those with a BMI of 25–29.9 kg/m^2 or a high waist circumference, unless they have two or more comorbidities.
- Combined therapy with a low-calorie diet (LCD), increased physical activity, and behavior therapy provide the most successful intervention for weight loss and weight maintenance.
- Consider pharmacotherapy only if a patient has not lost 1 pound per week after 6 months of combined lifestyle therapy.

The + represents the use of indicated treatment regardless of comorbidities.

Pharmacologic therapy for weight loss is not the first line of approach. First line is to initiate a multi-component lifestyle adjustment program. When the weight loss that occurs is unsatisfactory after 6 months, then weight management agents can be considered.

Lifestyle Therapy[3]

<Meal Plan>	<Physical Activity>	<Behavior>
• Reduced-calorie healthy meal plan • ~500–750 kcal daily deficit • Individualize based on personal and cultural preferences • Meal plans can include: Mediterranean, DASH, low-carb, low-fat, volumetric, high protein, vegetarian • Meal replacements • Very low-calorie diet is an option in selected patients and requires medical supervision Team member or expertise: dietitian, health educator	• Voluntary aerobic physical activity progressing to >150 minutes/week performed on 3–5 separate days per week • Resistance exercise: single-set repetitions involving major muscle groups, 2–3 times per week • Reduce sedentary behavior • Individualize program based on preferences and take into account physical limitations Team member or expertise: exercise trainer, physical activity coach, physical/occupational therapist	An interventional package that includes any number of the following: • Self-monitoring (food intake, exercise, weight) • Goal setting • Education (face-to-face meetings, group sessions, remote technologies) • Problem-solving strategies • Stimulus control • Behavioral contracting • Stress reduction • Psychological evaluation, counseling, and treatment when needed • Cognitive restructuring • Motivational interviewing • Mobilization of social support structures Team member or expertise: health educator, behaviorist, clinical psychologist, psychiatrist

National Institutes Of Health National Heart, Lung, And Blood Institute North American Association For The Study Of Obesity recommends pharmacotherapy as adjunct therapy in individuals with BMI ≥ 30 or ≥ 27 with other risk factors or diseases, such as waist circumference. AACE/ACE Obesity treatment guidelines indicates lower BMI range of ≤23 in certain ethnicities.

Although there is no specific guidelines to follow, as far as pharmacologic intervention is concerned, AACE/ACE recommends certain weight loss medications based on coexisting disease.

PREFERRED WEIGHT-LOSS MEDICATIONS: INDIVIDUALIZATION OF THERAPY

KEY: PREFERRED DRUG | USE WITH CAUTION | AVOID

CLINICAL CHARACTERISTICS OR CO-EXISTING DISEASES		MEDICATIONS FOR CHRONIC WEIGHT MANAGEMENT				
		Orlistat	Lorcaserin	Phentermine/ topiramate ER	Naltrexone ER/ bupropion ER	Liraglutide 3 mg
Diabetes Prevention (metabolic syndrome, prediabetes)			Insufficient data for T2DM prevention		Insufficient data for T2DM prevention	
Type 2 Diabetes Mellitus						
Hypertension				Monitor heart rate	Monitor BP and heart rate Contraindicated in uncontrolled HTN	Monitor heart rate
Cardiovascular Disease	CAD			Monitor heart rate	Monitor heart rate, BP	Monitor heart rate
	Arrhythmia		Monitor for bradycardia	Monitor heart rate, rhythm	Monitor heart rate, rhythm, BP	Monitor heart rate, rhythm
	CHF	Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Chronic Kidney Disease	Mild (50–79 mL/min)					
	Moderate (30–49 mL/min)			Do not exceed 7.5 mg/46 mg per day	Do not exceed 8 mg/90 mg bid	
	Severe (<30 mL/min)	Watch for oxalate nephropathy	Urinary clearance of drug metabolites	Urinary clearance of drug	Urinary clearance of drug	Avoid vomiting and volume depletion
Nephrolithiasis		Calcium oxalate stones		Calcium phosphate stones		
Hepatic Impairment	Mild-Moderate (Child-Pugh 5–9)	Watch for cholelithiasis	Hepatic metabolism of drug	Do not exceed 7.5 mg/46 mg per day	Do not exceed 8 mg/90 mg in AM	Watch for cholelithiasis
	Severe (Child-Pugh >9)	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Depression			Insufficient safety data Avoid combinations of serotonergic drugs	Avoid maximum dose: 15 mg/92 mg per day	Insufficient safety data Avoid in adolescents and young adults	
Anxiety				Avoid max dose: 15 mg/92 mg per day		
Psychoses		Insufficient data	Insufficient data	Insufficient data	Insufficient data	Insufficient data
Binge Eating Disorder			Insufficient data; however, possible benefit based on reduction in food cravings	Insufficient data; however, possible benefit based on studies with topiramate	Insufficient data, though possible benefit based on studies with bupropion Avoid in patients with purging or bulimia nervosa	Insufficient data
Glaucoma				Contraindicated, may trigger angle closure	May trigger angle closure	
Seizure Disorder				If discontinuing from max dose, taper slowly	Bupropion lowers seizure threshold	
Pancreatitis		Monitor for symptoms				Monitor for symptoms Avoid if prior or current disease
Opioid Use					Will antagonize opioids and opiates	
Women of Reproductive Potential	Pregnancy	Use contraception and discontinue orlistat should pregnancy occur	Use contraception and discontinue lorcaserin should pregnancy occur	Use contraception and discontinue phentermine/topiramate should pregnancy occur (perform monthly pregnancy checks to identify early pregnancy)	Use contraception and discontinue naltrexone ER/bupropion ER should pregnancy occur	Use contraception and discontinue liraglutide 3 mg should pregnancy occur
	Breast-feeding	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended
Age ≥65 years *		Limited data available	Insufficient data	Limited data available	Insufficient data	Limited data available
Alcoholism/ Addiction			Might have abuse potential due to euphoria at high doses	Insufficient data, though topiramate might exert therapeutic benefits	Avoid due to seizure risk and lower seizure threshold on bupropion	
Post-Bariatric Surgery		Insufficient data	Insufficient data	Limited data available	Insufficient data	Data available at 1.8 – 3.0 mg/day

* Use medications only with clear health-related goals in mind; assess patient for osteoporosis and sarcopenia.

Abbreviations: BP = blood pressure; CAD = coronary artery disease; CHF = congestive heart failure; HTN = hypertension; T2DM = Type 2 Diabetes Mellitus.

When weight loss achieved is not ≥5% within 3 to 6 months of treatment initiation, then it should be discontinued and another agent can be used. For HPSJ, the initial agent that can be used is phentermine. If treatment failure occurs on phentermine, Xenical will be recommended to be tried.

Triage:

- PA request must contain
  - BMI and comorbidities
  - Exercise and diet counseling by a registered dietician

EVALUATION CRITERIA FOR APPROVAL/EXCEPTION CONSIDERATION

Below are the coverage criteria and required information for each agent. These coverage criteria have been reviewed approved by the HPSJ Pharmacy & Therapeutics (P&T) Advisory Committee. For conditions not covered under this Coverage Policy, HPSJ will make the determination based on Medical Necessity as described in HPSJ Medical Review Guidelines (UM06).

Sympathomimetic
Phentermine (Adipex-P, Lomaira), Benzphetamine Hcl (Regimex), Diethylpropion Hcl (Tenuate), Phendimetrazine Tartrate (Bontril)

Phentermine

- ❒ **Coverage Criteria:** None
- ❒ **Limits:** None
- ❒ **Required Information for Approval:** None
- ❒ **Notes:**
  - Doses are individualized to achieve adequate responses with the lowest effective dose.
- ❒ **Non-formulary:** Suprenza ODT, Phentermine Capsules, Lomaira, Benzphetamine Hcl (Regimex), Diethylpropion Hcl (Tenuate), Phendimetrazine Tartrate (Bontril)

Lipase Inhibitor
Orlistat (Xenical, Alli)

Orlistat (Xenical, Alli)

- ❒ **Coverage Criteria:**
  - Weight loss agents are reserved for patients with Body Mass Index > 30 or ≥27 with > 2 comorbidities AND had received exercise and dietary counseling at least twice by a registered dietitian.
- ❒ **Limits:** None
- ❒ **Required Information for Approval:**
  - Documentation of BMI and comorbidities.
  - Documentation of exercise and dietary counseling at least twice by a registered dietician.
  - Initial approval: 3 months
  - Continuation of therapy: 3 months at a time
    - Documentation of ≥5% weight loss via clinic notes that contain the patient's updated BMI or height and weight.
- ❒ **Notes:**
  - Dose modification must occur if patient is also taking cyclosporine or levothyroxine.
  - Alli and Xenical are administered 3 times daily with each main meal that contains fat. Doses must be omitted if a meal is missed or the meal does not contain fat.

Serotonin 5-HT2C Receptor Agonist
Lorcaserin Hcl (Belviq)

- ❒ **Non-formulary**

GLP-1 Agonist
Liraglutide (Saxenda)

- ❒ **Non-formulary**

Opioid Antagonist-Dopamine/Norepin-ephrine Reuptake Inhibitor
Bupropion/Naltrexone (Contrave)

❒ **Non-formulary**

Combination
Phentermine/Topiramate (Qsymia)

❒ **Non-formulary**

REFERENCES

1. Xenical® [prescribing information]. South San Francisco, CA: Genentech, CA; 2015.
2. The Practical Guide Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. National Institutes Of Health National Heart, Lung, And Blood Institute North American Association For The Study Of Obesity. https://www.nhlbi.nih.gov/files/docs/guidelines/prctgd_c.pdf
3. Garvey t., Mechanick J. Brett E. et al., American Association Of Clinical Endocrinologists And American College Of Endocrinology Comprehensive Clinical Practice Guidelines For Medical Care Of Patients With Obesity. Endocrine Practice Vol 22 (Suppl 3) July 2016.
4. Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab*. 2015;100(2):342-362.[PubMed 25590212]
5. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society [published online November 7, 2013]. *J Am Coll Cardiol*.[PubMed 24239920]

REVIEW & EDIT HISTORY

Document Changes	Reference	Date	P&T Chairman
Creation of Policy	HPSJ Coverage Policy – Gastrointestinal Disorders – Weight Loss 2016-05.docx	5/2016	Johnathan Yeh, PharmD
Update Policy	HPSJ Coverage Policy – Gastrointestinal Disorders – Weight Loss 2017-05.docx	5/2017	Johnathan Yeh, PharmD
Update Policy	HPSJ Coverage Policy – Gastrointestinal Disorders – Weight Loss 2018-09.docx	9/2018	Johnathan Yeh, PharmD
Review Policy	Weight Loss	9/2019	Matthew Garrett, PharmD
Review Policy	Weight Loss	9/2020	Matthew Garrett, PharmD
Review Policy	Weight Loss	9/2021	Matthew Garrett, PharmD

Note: All changes are approved by the HPSJ P&T Committee before incorporation into the utilization policy