Prior Authorization
Weight Loss – Other Appetite Suppressants and Xenical

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Product Identifier(s)

12888, 51169, 51170, 51171

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

National Formulary Medical Necessity

Drugs Affected

- Adipex-P® (phentermine hydrochloride capsules and tablets, generics)
- benzphetamine hydrochloride tablets (generics only)
- Contrave® (naltrexone HCl/buproprion HCl extended-release tablets)
- diethylpropion hydrochloride immediate-release and controlled-release tablets (generics only)
- Lomaira™ (phentermine hydrochloride tablets)
- phendimetrazine tartrate tablets (generics only)
- phentermine hydrochloride orally disintegrating tablets (generics only)
- Regimex (benzphetamine 25 mg tablets, generics – obsolete 1/15/2019)
- Qsymia™ (phentermine and topiramate extended-release capsules
- Xenical® (orlistat 120 mg capsules)

Cigna covers Weight Loss – Other Appetite Suppressants and Xenical as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

Prior Authorization is recommended for prescription benefit coverage of benzphetamine, diethylpropion, phendimetrazine tartrate, phentermine hydrochloride, Qsymia, Contrave, and Xenical. All approvals are provided for the durations noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

Prior Authorization and prescription benefit coverage is not recommended for Alli® (orlistat 60 mg capsules).

FDA Indication(s)

I. Coverage of benzphetamine (including Regimax 25 mg tablets [generic]), diethylpropion, phendimetrazine tartrate, or phentermine hydrochloride is recommended in those who meet the following criteria:

1. Weight Loss. Approve for the duration noted if the individual meets one of the following criteria (A or B):
- **A)** Initial Therapy. Approve for 3 months if the individual meets all of the following criteria (i, ii, iii, and iv):
  - **i.** Individual is ≥ 16 years of age; AND
  - **ii.** Individual currently has a body mass index (BMI) ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with comorbidities besides obesity; AND
    Note: Examples of comorbidities include diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea.
  - **iii.** Individual has engaged in a trial of behavioral modification and dietary restriction for at least 3 months and has failed to achieve the desired weight loss; AND
  - **iv.** Individual is currently engaged in behavioral modification and on a reduced calorie diet.
- **B)** Individual is Continuing Therapy. Approve for 1 year if the individual meets all of the following criteria (i, ii, iii, and iv):
  Note: For an individual who has not completed 3 months of initial therapy, criterion (1A) must be met (do not use continuation criteria if the initial 3 months were not completed).
  - **i.** Individual is ≥ 16 years of age; AND
  - **ii.** Individual had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with comorbidities besides obesity: AND
    Note: Examples of comorbidities include diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea.
  - **iii.** Individual is currently engaged in behavioral modification and on a reduced calorie diet; AND
  - **iv.** Individual has lost ≥ 5% of baseline body weight.

II. Coverage of Contrave is recommended in those who meet the following criteria:

1. Weight Loss. Approve for the duration noted if the individual meets one of the following criteria (A or B):
- **A)** Initial Therapy. Approve for 4 months if the individual meets the following criteria (i, ii, iii, and iv):
  - **i.** Individual is ≥ 18 years of age; AND
  - **ii.** Individual currently has a body mass index (BMI) ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with comorbidities besides obesity; AND
    Note: Examples of comorbidities include diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea.
  - **iii.** Individual has engaged in a trial of behavioral modification and dietary restriction for at least 3 months and has failed to achieve the desired weight loss; AND
  - **iv.** Individual is currently engaged in behavioral modification and on a reduced calorie diet.
- **B)** Individual is Continuing Therapy. Approve for 1 year if the individual meets the following criteria (i, ii, iii, and iv):
  Note: For an individual who has not completed 4 months of initial therapy, criterion (1A) must be met (do not use continuation criteria if the initial 4 months were not completed).
  - **i.** Individual is ≥ 18 years of age; AND
  - **ii.** Individual had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with comorbidities besides obesity: AND

Note: Examples of comorbidities include diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea.

iii. Individual is currently engaged in behavioral modification and on a reduced calorie diet; AND

iv. Individual has lost ≥ 5% of baseline body weight.

III. Coverage of Qsymia is recommended in those who meet the following criteria:

1. Weight Loss. Approve for the duration noted if the individual meets one of the following criteria (A or B):

A) Initial Therapy. Approve for 6 months if the individual meets the following criteria (i, ii, iii, and iv):

i. Individual is ≥ 18 years of age; AND

ii. Individual currently has a BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with comorbidities besides obesity; AND

Note: Examples of comorbidities include diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea.

iii. Individual has engaged in a trial of behavioral modification and dietary restriction for at least 3 months and has failed to achieve the desired weight loss; AND

iv. Individual is currently engaged in behavioral modification and on a reduced calorie diet.

B) Individual is Continuing Therapy. Approve for 1 year if the individual meets the following criteria (i, ii, iii, and iv):

Note: For an individual who has not completed 6 months of initial therapy, criterion (1A) must be met (do not use continuation criteria if the initial 6 months were not completed).

i. Individual is ≥ 18 years of age; AND

ii. Individual had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with comorbidities besides obesity; AND

Note: Examples of comorbidities include diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea.

iii. Individual is currently engaged in behavioral modification and on a reduced calorie diet; AND

iv. Individual has lost ≥ 5% of baseline body weight.

IV. Coverage of Xenical is recommended in those who meet one of the following criteria:

1. Weight Loss, Adult. Approve for the duration noted if the individual meets one of the following (A or B):

A) Initial Therapy. Approve for 3 months if the individual meets the following criteria (i, ii, iii, and iv):

i. Individual is ≥ 18 years of age; AND

ii. Individual meets ONE of the following (a or b):

a) Individual currently has a BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with comorbidities besides obesity; OR

Note: Examples of comorbidities include diabetes, dyslipidemia, hypertension, coronary heart disease, sleep apnea.

b) Individual had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with comorbidities besides obesity if maintaining weight loss after using a low calorie diet; AND

Note: Examples of comorbidities include diabetes, dyslipidemia, hypertension, coronary heart disease, sleep apnea.

iii. Individual has engaged in a trial of behavioral modification and dietary restriction for at least 3 months and has failed to achieve the desired weight loss; AND

iv. Individual is currently engaged in behavioral modification and on a reduced calorie diet.

B) Individual is Continuing Therapy. Approve for 1 year if the individual meets the following criteria (i, ii, iii, and iv):

Note: For an individual who has not completed 3 months of initial therapy, criterion (1A) must be met (do not use continuation criteria if the initial 3 months were not completed).

i. Individual is ≥ 18 years of age; AND

ii. Individual had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with comorbidities besides obesity: AND

Note: Examples of comorbidities include diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea.

iii. Individual is currently engaged in behavioral modification and on a reduced calorie diet; AND

iv. Individual has lost ≥ 5% of baseline body weight.

2. **Weight Loss, Pediatric.** Approve for the duration noted if the individual meets one of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 3 months if the individual meets the following criteria (i, ii, iii, and iv):
     - **i.** Individual is ≥ 12 years of age and < 18 years of age; AND
     - **ii.** Individual currently has a BMI of ≥ 95th percentile for age and sex, or in ≥ 85th percentile but < 95th percentile for age and sex and has at least one comorbidity (type 2 diabetes mellitus, cardiovascular disease [CVD]) or has a strong family history of type 2 diabetes or premature CVD; AND
       Note: Premature cardiovascular disease is defined as cardiovascular disease occurring in a male < 55 years of age or in a female < 65 years of age.
     - **iii.** Individual has engaged in a trial of behavioral modification and dietary restriction for at least 3 months and has failed to limit weight gain or to modify comorbidities; AND
     - **iv.** Individual is currently engaged in behavioral modification and on a reduced calorie diet.
   - **B)** Individual is Continuing Therapy. Approve for 12 months if the individual meets the following criteria (i, ii, iii, iv, and iv):
     Note: For an individual who has not completed 3 months of initial therapy, criterion (2A) must be met (do not use continuation criteria if the initial 3 months were not completed).
     - **i.** Individual is ≥ 12 years of age and < 18 years of age; AND
     - **ii.** Individual had an initial BMI of ≥ 95th percentile for age and sex, or ≥ 85th percentile but < 95th percentile for age and sex and has at least one comorbidity (type 2 diabetes or CVD) or strong family history of type 2 diabetes or premature CVD; AND
       Note: Premature cardiovascular disease is defined as cardiovascular disease occurring in a male < 55 years of age or in a female < 65 years of age.
     - **iii.** Individual is currently engaged in behavioral modification and on a reduced calorie diet; AND
     - **iv.** Individual's current BMI percentile has decreased for age and weight (taking into account that the individual is increasing in height and will have a different normative BMI from when Xenical was started); AND
     - **v.** Individual currently has a BMI > 85th percentile.

Conditions Not Covered

Benzphetamine, diethylpropion, phendimetrazine tartrate, phentermine hydrochloride, Qsymia, Contrave, and Xenical are considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

1. **Concomitant Use with Other Weight Loss Medications.** Concomitant use with other medications intended for weight loss is not recommended. Of note, examples of medications FDA-approved for weight loss include phentermine, benzphetamine, diethylpropion, phendimetrazine, Contrave, Qsymia, Xenical, Saxenda (liraglutide subcutaneous injection), and Wegovy (semaglutide subcutaneous injection). Additionally, Alli (orlistat 60 mg capsules) is available over-the-counter.

Background

Overview

The appetite suppressant products vary slightly in the wording of their FDA-approved indications.

- **Benzphetamine**, **diethylpropion**, and **phendimetrazine** are indicated for the management of exogenous obesity as a short-term adjunct (a few weeks) to a regimen of weight reduction based on caloric restriction in patients with an initial body mass index (BMI) of ≥ 30 kg/m^2 who have not responded to a weight reducing regimen (diet and/or exercise) alone.[1-3]
- **Phentermine** hydrochloride is indicated for short-term (a few weeks) adjunctive therapy in a regimen of weight reduction based on exercise, behavioral modification and caloric restriction in the management of exogenous obesity in those with an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 when other risk factors are present (e.g., controlled hypertension, diabetes mellitus, or dyslipidemia).[4-6]

- **Qsymia** and **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 of ≥ 30 kg/m^2 (obese), or ≥ 27 kg/m^2 (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes).[7,8]
- **Xenical** is indicated for obesity management including weight loss and weight maintenance when used in conjunction with a reduced-calorie diet in patients with an initial body mass index ≥ 30 kg/m^2, or ≥ 27 kg/m^2 in the presence of at least one weight-related comorbidity (e.g., hypertension, diabetes, dyslipidemia), and to reduce the risk for weight gain after prior weight loss.[9]

Contrave
The recommended maintenance dose of Contrave is achieved at Week 4.[8] Response to therapy should be evaluated after 12 weeks at the maintenance dosage (Week 16, if dosed according to the prescribing information). If a patient has not lost ≥ 5% of baseline body weight, discontinue Contrave, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

Qsymia
Response to therapy should be evaluated by Week 12.[7] If a patient has not lost ≥ 3% of baseline body weight, discontinue Qsymia or escalate the dose. If a patient has not lost ≥ 5% of baseline body weight after an additional 12 weeks of treatment on the escalated dose, discontinue Qsymia as directed as it is unlikely the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

Guidelines
Guidelines from the Endocrine Society regarding pharmacological management of obesity (2015) recommend pharmacotherapy as adjunct to behavioral modification to reduce food intake and increase physical activity for patients with BMI ≥ 30 kg/m^2 or ≥ 27 kg/m^2 in the presence of at least one comorbidity, such as hypertension, dyslipidemia, type 2 diabetes, or obstructive sleep apnea.[10] If a patient's response to a weight loss medication is deemed effective (weight loss ≥ 5% of body weight at 3 months) and safe, it is recommended that the medication be continued. Although the noradrenergic weight loss medications are only labeled for short-term use, the Endocrine Society notes that off-label, long-term prescribing of phentermine is reasonable for most patients, as long as the patient has been informed that other medications for weight loss are FDA-approved for long-term use.

Per American Association of Clinical Endocrinologists/American College of Endocrinology obesity guidelines (2016), pharmacotherapy for overweight and obesity should be used only as an adjunct to lifestyle therapy and not alone.[11] The addition of pharmacotherapy produces greater weight loss and weight-loss maintenance compared with lifestyle therapy alone. The concurrent initiation of lifestyle therapy and pharmacotherapy should be considered in patients with weight-related complications that can be ameliorated by weight loss. Pharmacotherapy should be offered to patients with obesity, when potential benefits outweigh the risks, for the chronic treatment of the disease. Short-term treatment (3 to 6 months) using weight-loss medications has not been demonstrated to produce longer-term health benefits and cannot be generally recommended based on scientific evidence.

Guidelines in Pediatric Obesity
A 2017 Endocrine Society clinical practice guideline on pediatric obesity recommends pharmacotherapy in combination with lifestyle modification be considered in obese children or adolescents only after failure of a formal program of intensive lifestyle (dietary, physical activity and behavioral) modification to limit weight gain or to ameliorate comorbidities.[12] The Endocrine Society recommends pharmacotherapy in overweight children and adolescents < 16 years only in the context of a clinical trial. Pharmacotherapy should be provided only by clinicians who are experienced in the use of anti-obesity agents and aware of the potential for adverse events. These guidelines recommend limited use of pharmacotherapy because pediatric obesity should be managed preferably as a serious lifestyle condition with important lifelong consequences.

The Endocrine Society defines overweight as BMI in at least the 85th percentile but less than the 95th percentile, and obesity as BMI in at least the 95th percentile for age and sex against routine endocrine studies, unless the height velocity is attenuated or inappropriate for the family background or stage of puberty.

References

1. Benzphetamine hydrochloride tablets [prescribing information]. Newtown, PA: KVK-Tech; March 2021.
2. Diethylpropion immediate release and controlled release tablets [prescribing information]. Philadelphia, PA: Lannett; December 2019.
3. Phendimetrazine tablets [prescribing information]. Northvale, NJ: Elite Laboratories; February 2019.
4. Adipex-P® tablets and capsules [prescribing information]. Horsham, PA: Teva Pharmaceuticals; March 2017.
5. Lomaira™ tablets [prescribing information]. Newtown, PA: KVK-Tech; September 2016.
6. Phentermine ODT [prescribing information]. Pennington, NJ: Zydus Pharmaceuticals; February 2014.
7. Qsymia® capsules [prescribing information]. Mountain View, CA: Vivus, Inc.; October 2020.
8. Contrave® tablets [prescribing information]. La Jolla, CA: Orexigen Therapeutics; June 2018.
9. Xenical capsules [prescribing information]. Nutley, NJ: Roche Laboratories; August 2017.
10. Apovian CM, Aronne LJ, Bessesen DH, McDonnell ME, Murad MH, Pagotto U, Ryan DH, Still CD; Endocrine Society. Pharmacological management of obesity: an endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2015 Feb;100(2):342-62.
11. Garvey WT, Mechanick JI, Brett EM, Garber AJ, Hurley DL, Jastreboff AM, Nadolsky K, Pessah-Pollack R, Plodkowski R; Reviewers of the AACE/ACE Obesity Clinical Practice Guidelines. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract*. 2016 Jul;22 Suppl 3:1-203.
12. Styne DM, Arslanian SA, Connor EL, Farooqi IS, Murad MH, Silverstein JH, Yanovski JA. Pediatric Obesity-Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2017 Mar 1;102(3):709-757.

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	<u>Benzphetamine, diethylpropion, phendimetrazine, phentermine, Contrave, and Qsymia:</u> **Weight Loss:** The age criterion was moved from the approval condition into criteria. References to a Body Mass Index (BMI) chart were removed. <u>Xenical</u>: **Weight Loss, Adult:** The condition was reworded as listed, previously this was titled "Weight Loss in Patients ≥ 18 Years of Age". The age criterion was moved from the approval condition into criteria. References to a BMI chart were removed. **Weight Loss, Pediatric:** The condition was reworded as listed, previously this was titled "Weight Loss in Patients Aged ≥ 12 to < 18 Years." The age criterion was moved from the approval condition into criteria. References to a BMI chart were removed. <u>Conditions Not Recommended for Approval</u>: **Concomitant Use with Other Weight Loss Medications:** The Condition Not Recommended for Approval was reworded to as listed; previously, "Combination Appetite Suppressant Therapy" and "Simultaneous Use of Xenical with any of the Following: benzphetamine, diethylpropion, phendimetrazine tartrate, phentermine hydrochloride or resin, Contrave, Saxenda, or Qsymia" were listed as two separate Conditions Not Recommended for Approval. **Treatment of Hyperlipidemia in Non-Obese Patients:** The Condition Not Recommended for Approval was removed from the policy. **Treatment of Binge-Eating Disorder in Non-Obese Patients (BMI < 30 kg/m^2 or < 27 kg/m^2 for Those with Risk Factors):** The Condition Not Recommended for Approval was removed from the policy. **Prevention of Diabetes in Patients with BMI < 30 kg/m^2:** The Condition Not Recommended for Approval was removed from the policy.	12/15/2021

	Nonalcoholic Fatty Liver Disease: The Condition Not Recommended for Approval was removed from the policy.	