EXPRESS SCRIPTS®

PRIOR AUTHORIZATION POLICY

POLICY: Weight Loss Drugs

- Adipex-P® (phentermine hydrochloride capsules and tablets – Teva, generics)
- Belviq® (lorcaserin hydrochloride tablets − Arena/Eisai, Inc.)
- Belviq® XR (lorcaserin hydrochloride extended-release tablets – Arena/Eisai, Inc.)
- benzphetamine hydrochloride tablets (generics only)
- Bontril® PDM, (phendimetrazine tartrate tablets – Valeant Pharmaceuticals, generics – obsolete 1/20/2016)
- Contrave® (naltrexone HCl/buproprion HCl extended-release tablets – Orexigen Therapeutics)
- diethylpropion hydrochloride immediate-release and controlled-release tablets (generics only)
- Lomaira™ (phentermine hydrochloride tablets – KVK-Tech)
- Regimex (benzphetamine 25 mg tablets – WraSer Pharmaceuticals, generics)
- Saxenda® (liraglutide [rDNA] injection – NovoNordisk)
- Suprenza™ (phentermine hydrochloride orally disintegrating tablets – Akrimax Pharmaceuticals, generics – obsolete 7/01/2016)
- Qsymia™ (phentermine and topiramate extended-release capsules – Vivus, Inc.)
- Xenical® (orlistat 120 mg capsules − Roche)

TAC REVIEW DATE: 10/24/2018

OVERVIEW

This policy is limited to prescription medications that are indicated to promote weight loss in obese patients. Obesity in adults is defined as a body mass index (BMI) of ≥ 30 kg/m^2; a BMI of 25 to 29.9 kg/m^2 is termed overweight.[1] The combined prevalence of obesity and overweight is estimated at > 64% of US adults; 4.7% of adults have a BMI ≥ 40 kg/m^2. In the US, an estimated 300,000 adult deaths per year are due to obesity-related causes. With the increase in obesity, treatments for obesity have increased in number and are more commonly used. Diet therapy with a low calorie diet, increased physical activity, and behavioral modification are the mainstays of treatment of overweight and obese adults. Such a regimen should be maintained for at least 6 months before considering pharmacotherapy. The rationale for adding drug therapy to these regimens in selected adults is that a more successful weight loss and maintenance may result.[2-3] Weight loss goals should be individually determined and these goals may include not just weight loss but other parameters, such as improved glucose metabolism, lipid levels, and blood pressure.[1]

Drugs that are indicated for weight loss either: 1) decrease food intake by decreasing appetite or increasing satiety (appetite suppressant, anorectic), or 2) decrease nutrient absorption.[4] The appetite suppressants increase the availability of anorexigenic neurotransmitters (norepinephrine, serotonin, dopamine, or some combination of these) in the central nervous system (CNS). Appetite suppressant products currently available are as follows:

- benzphetamine hydrochloride (Regimex and generic products) C-III [noradrenergic][5,33]
- diethylpropion hydrochloride (generic products) C-IV [noradrenergic][6]
- phendimetrazine tartrate (Bontril PDM and generic products) C-III [noradrenergic][7]

- phentermine hydrochloride (Adipex-P, Lomaira, Suprenza, and generic products) C-IV [noradrenergic][8-9,32]
- Belviq/Belviq XR (serotonin 2C ([5-HT_{2C}] receptor agonist)[10]
- Qsymia (anorectic and antiepileptic) C-IV[11]
- Contrave (opioid antagonist and antidepressant)[28]
- Saxenda (glucagon-like peptide-1 agonist)[29]

The other commercially available weight loss product, orlistat, acts by inhibiting the absorption of dietary fats and is not an appetite suppressant.[12] Orlistat is available by prescription as Xenical, and over-the-counter (OTC) as Alli® (orlistat 60 mg capsules). Alli is not included within the scope of this policy.

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 BMI of ≥ 30 kg/m^2 who have not responded to a weight reducing regimen (diet and/or exercise) alone.[5-7,33] 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).[8-9,32] Belviq/Belviq XR, Qsymia, Contrave, and Saxenda 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).[10-11,28-29]

Xenical

Xenical is indicated for obesity management including weight loss and weight maintenance when used in conjunction with a reduced calorie diet.[12] Xenical is also indicated to reduce the risk for weight regain after prior weight loss. Xenical is indicated for obese patients with an initial BMI ≥ 30 kg/m^2 or ≥ 27 kg/m^2 in the presence of other risk factors (e.g., hypertension, diabetes, dyslipidemia).[12] Xenical has been used effectively to further reduce weight, maintain weight loss, or prevent as much regain in patients (BMI initially 28 to 43 kg/m^2) who initially lost weight on a 6-month low calorie diet.[13] In another study, patients who lost ≥ 5% of their body weight on an 8-week very-low-calorie diet (n = 309) were randomized to receive Xenical or placebo for 3 years, plus lifestyle counseling.[14] The mean weight gain after 3 years was 4.6 kg with Xenical and 7.0 kg with placebo (P < 0.02). The incidence of new cases of type 2 diabetes was reduced in the Xenical group (n = 8/153) vs. placebo (n = 17/156) [P = 0.04].

The XENical in the prevention of Diabetes in Obese Subjects (XENDOS) study was a 4-year, double-blind, prospective trial that randomized 3,305 patients to lifestyle changes plus either Xenical 120 mg TID with meals or placebo.[15] The primary study outcomes were the onset of type 2 diabetes and body weight changes. Patients (30 to 60 years of age) were nondiabetic and had a BMI ≥ 30 kg/m^2. Most patients had normal glucose tolerance, but some had impaired glucose tolerance (79% and 21% of patients, respectively). Lifestyle changes and a reduced calorie diet were also implemented. Of the patients randomized to Xenical, 52% completed 4 years of treatment vs. 34% of patients randomized to placebo. The mean weight loss with Xenical at 4 years was greater (5.8 kg) compared with placebo (3.0 kg; P < 0.001). After 4 years of therapy, fewer patients randomized to Xenical progressed to having type 2 diabetes compared with placebo (P = 0.0032) [cumulative 4-year incidence rates of 6.2% {Xenical} and 9.0% {placebo}] (risk reduction of 37.3%). The reduction in the development of type 2 diabetes with Xenical was more marked in patients with impaired glucose tolerance at baseline (18.8% with Xenical vs. 28.8% with placebo) corresponding to a 45% risk reduction. Xenical did not reduce the risk of developing diabetes in patients with normal glucose

tolerance at baseline.[12] The effect of Xenical to delay the onset of type 2 diabetes in obese patients with impaired glucose tolerance is presumably due to weight loss and not to an independent effect(s) of the drug on glucose or insulin metabolism.

Use of Xenical in Obese or Overweight Pediatric Patients

In a 54-week trial, 539 adolescents (12 to 16 years of age with BMI ≥ 2 units above the 95th percentile; maximum BMI of 44 kg/m^2) were randomized to Xenical 120 mg TID or placebo.[12,16] Both groups were on a mildly hypocaloric diet, exercise and behavioral therapy. In all, 190 patients dropped out. Both groups had a decrease in BMI up to 12 weeks. At 54 weeks, the mean BMI decreased from baseline by -0.55 kg/m^2 with Xenical and increased by +0.31 kg/m^2 with placebo (P = 0.001); weight increased by +0.53 kg with Xenical and by +3.14 kg with placebo (P < 0.001). In a 6-month double-blind trial, 40 adolescents (14 to 18 years of age) were randomized to Xenical 120 mg TID (mean BMI 39.2 kg/m^2) or placebo (mean BMI 41.7 kg/m^2).[17] Patients received dietary and exercise counseling. No statistically significant difference was noted between the two study groups for decrease in BMI from baseline to 6 months (P = 0.39), the primary end point. The BMI decreased within the Xenical group (-1.3 ± 1.6 kg/m^2; P = 0.04) and within the placebo group (-0.8 ± 3.0 kg/m^2; P = 0.02) which was statistically significant. The Xenical group had increased adverse events compared to placebo, primarily gastrointestinal symptoms.

The most commonly used pharmacotherapeutic agents in pediatric patients are sibutramine (prior to withdrawal from the US market), orlistat, and metformin (note that metformin is not indicated for the treatment of obesity).[18] A meta-analysis, commissioned by the Endocrine Society task force, showed that sibutramine demonstrated the greatest effect with a decrease in BMI of -2.4 kg/m^2 (95% confidence interval [CI]: 1.8, 3.1 kg/m^2) after 6 months, but patients had a greater increase in blood pressure and pulse rate than with placebo.[21] Orlistat produced a significant decrease in BMI of -0.7 kg/m^2 (95% CI: 0.3, 1.2 mg/m^2) but there were increased gastrointestinal adverse events (abdominal discomfort, pain, and steatorrhea). Orlistat has reduced utility in children since it must be taken with each meal and children are often in school at lunchtime.[18] Metformin monotherapy decreased BMI in hyperinsulinemic, non-diabetic obese adolescents slightly but significantly in each of the studies analyzed. The overall effect did not reach statistical significance in the meta-analysis. Metformin is indicated for type 2 diabetes mellitus in children ≥ 10 years of age. The Endocrine Society guidelines recommend that use of agents that are not indicated for obesity (e.g., metformin, octreotide, leptin, topiramate, growth hormone) should be restricted to large, well-controlled studies.

Guidelines

The Endocrine Society published a clinical practice guideline (2015) for the pharmacological management of obesity.[30] The guidelines recommend that pharmacotherapy be employed for patients with BMI ≥ 27 kg/m^2 with comorbidity or BMI > 40 kg/m^2) as adjuncts to behavioral modification to reduce food intake and increase physical activity when possible. The Society states that patients who have a history of being unable to successfully lose and maintain weight and who meet label indications are candidates for weight-loss medication. Safety and efficacy is recommended to be assessed monthly for the first three months, and then at least every 3 months in all patients prescribed medications for weight loss. If a patient has an adequate response to weight loss medication (weight loss ≥ 5% at 3 months), medication is recommended to be continued. If deemed to be ineffective (weight loss < 5% at 3 months) or if there are safety or tolerability issues at any time, it is recommended that medication be discontinued and alternative medications or referral for alternative treatment approaches be considered.

The American Association of Clinical Endocrinology (AACE)/American College of Endocrinology (ACE) guidelines for medical care of patients with obesity (2016) recommend pharmacotherapy for overweight and obese patients only as an adjunct to lifestyle therapy.[31] Pharmacotherapy should be offered to patients

who are obsess when the potential benefits outweigh the risks, for the chronic treatment of obesity. Short-term (3 to 6 months) use of weight-loss medications has not been demonstrated to produce longer-term health benefits and cannot be generally recommended.

Guidelines in Pediatric Obesity

A 2008 Endocrine Society practice guideline on pediatric obesity recommends pharmacotherapy in combination with lifestyle modification be considered in the following population: 1) obese children only after failure of a formal program of intensive lifestyle [dietary, physical activity and behavioral] modification; and 2) overweight children only if severe co-morbidities persist despite intensive lifestyle modification, particularly in children with a strong family history of type 2 diabetes or premature cardiovascular disease.[18] Patients with a genetic syndrome etiology should be referred to a geneticist. Pharmacotherapy should be provided only by clinicians who are experienced in the use of antiobesity 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.[18] The Centers for Disease Control (CDC) derived normative percentiles are recommended as the appropriate method for determining the BMI in children.[19-20]

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of benzphetamine, diethylpropion, phendimetrazine tartrate, phentermine hydrochloride, Belviq, Belviq XR, Qsymia, Contrave, Saxenda, and Xenical. All approvals are provided for the durations noted below.

Prior authorization and prescription benefit coverage is not recommended for Alli.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. Weight Loss in Adults or Adolescents ≥ 16 Years of Age. Note: For individuals who have not completed the initial 3 months of therapy, criterion 1, A must be met (do not use continuation criteria if the initial 3 months were not completed).

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

i. Patient currently has a body mass index (BMI) ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea) [Appendix A contains a BMI chart]; AND

ii. Patient 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
iii. Patient is currently engaged in behavioral modification and on a reduced calorie diet.

B) Patients Continuing Therapy. Approve for 12 months if the patient meets all of the following criteria (i, ii, and iii):
i. Patient had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea); AND
ii. Patient is currently engaged in behavioral modification and on a reduced calorie diet; AND
iii. Patient has lost ≥ 5% of baseline body weight.

Although the noradrenergic weight loss medications are only labeled for short-term use, the Endocrine Society (2015) 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.[30] According to prescribing information, safety and efficacy have not been established for diethylpropion and phentermine (hydrochloride or resin) in children younger than 16 years,[6,8,9,32] and for benzphetamine, phendimetrazine and Xenical in children < 12 years of age.[5,7,12,33] However, the Endocrine Society has established guidelines for use of Xenical in pediatric patients.[18] Benzphetamine, diethylpropion, phendimetrazine and phentermine are not included in these guidelines.

II. Coverage of Belviq or Belviq XR is recommended in those who meet all of the following criteria:

FDA-Approved Indications

1. **Weight Loss in Adults ≥ 18 years of Age.** Note: For individuals who have not completed the initial 3 months of therapy, criterion 1, A must be met (do not use continuation criteria if the initial 3 months were not completed).
A) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i, ii, and iii):
i. Patient currently has a BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea) [Appendix A contains a BMI chart]; AND
ii. Patient 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
iii. Patient is currently engaged in behavioral modification and on a reduced calorie diet.
B) Patients Continuing Therapy. Approve for 12 months if the patient meets the following criteria (i, ii, and iii):
i. Patient had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea); AND
ii. Patient is currently engaged in behavioral modification and on a reduced calorie diet; AND
iii. Patient has lost ≥ 5% of baseline body weight.

According to the prescribing information, the response to therapy should be evaluated by Week 12.[10] If a patient has not lost ≥ 5% of baseline body weight, discontinue Belviq, as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

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

FDA-Approved Indications

1. **Weight Loss in Adults ≥ 18 Years of Age.** Note: For individuals who have not completed the initial 4 months of therapy, criterion 1, A must be met (do not use continuation criteria if the initial 4 months were not completed).
   - **A)** Initial Therapy. Approve for 4 months if the patient meets the following criteria (i, ii, and iii):
     - **i.** Patient currently has a BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea) [Appendix A contains a BMI chart]; AND
     - **ii.** Patient 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
     - **iii.** Patient is currently engaged in behavioral modification and on a reduced calorie diet.
   - **B)** Patients Continuing Therapy. Approve for 12 months if the patient meets the following criteria (i, ii, and iii):
     - **i.** Patient had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea); AND
     - **ii.** Patient is currently engaged in behavioral modification and on a reduced calorie diet; AND
     - **iii.** Patient has lost ≥ 5% of baseline body weight.

   The recommended maintenance dose of Contrave is achieved at Week 4.[28] 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.

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

FDA-Approved Indications

1. **Weight Loss in Adults ≥ 18 Years of Age.** Note: For individuals who have not completed the initial 6 months of therapy, criterion 1, A must be met (do not use continuation criteria if the initial 6 months were not completed).
   - **A)** Initial Therapy. Approve for 6 months if the patient meets the following criteria (i, ii, and iii):
     - **i.** Patient currently has a BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea) [Appendix A contains a BMI chart]; AND
     - **ii.** Patient 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
     - **iii.** Patient is currently engaged in behavioral modification and on a reduced calorie diet.
   - **B)** Patients Continuing Therapy. Approve for 12 months if the patient meets the following criteria (i, ii, and iii):
     - **i.** Patient had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea); AND
     - **ii.** Patient is currently engaged in behavioral modification and on a reduced calorie diet; AND
     - **iii.** Patient has lost ≥ 5% of baseline body weight.

Response to therapy should be evaluated by Week 12.[11] 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.

V. Coverage of Saxenda is recommended in those who meet all of the following criteria:

1. Weight Loss in Adults ≥ 18 years of Age. Note: For individuals who have not completed the initial 4 months of therapy, criterion 1, A must be met (do not use continuation criteria if the initial 4 months were not completed).

A) Initial Therapy. Approve for 4 months if the patients meets the following criteria (i, ii, and iii):

i. Patient currently has a BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea) [Appendix A contains a BMI chart]; AND

ii. Patient 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

iii. Patient is currently engaged in behavioral modification and on a reduced calorie diet.

B) Patients Continuing Therapy. Approve for 12 months if the patient meets the following criteria (i, ii, and iii):

i. Patient had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea); AND

ii. Patient is currently engaged in behavioral modification and on a reduced calorie diet; AND

iii. Patient has lost ≥ 4% of baseline body weight.

The change in body weight with Saxenda should be evaluated 16 weeks after initiating Saxenda.[29] If the patient has not lost ≥ 4% of baseline body weight, Saxenda should be discontinued because it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment.

VI. Coverage of Xenical is recommended in those who meet all of the following criteria:

FDA-Approved Indications

1. Weight Loss in Adults ≥ 18 Years of Age. Note: For individuals who have not completed the initial 3 months of therapy, criterion 1, A must be met (do not use continuation criteria if the initial 3 months were not completed).

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

i. Patient meets ONE of the following (a or b):

a) Patient currently has a BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes, dyslipidemia, hypertension, coronary heart disease, sleep apnea) [Appendix A contains a BMI chart]; OR

b) Patient had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes, dyslipidemia, hypertension, coronary heart disease, sleep apnea) if maintaining weight loss after using a low calorie diet; AND

ii. Patient 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
iii. Patient is currently engaged in behavioral modification and on a reduced calorie diet.

B) Patients Continuing Therapy. Approve for 12 months if the patient meets the following criteria (i, ii, and iii):
i. Patient had an initial BMI ≥ 30 kg/m^2, or a BMI ≥ 27 kg/m^2 for those with risk factors besides obesity (e.g., diabetes mellitus, impaired glucose tolerance, dyslipidemia, hypertension, coronary heart disease, sleep apnea); AND
ii. Patient is currently engaged in behavioral modification and on a reduced calorie diet; AND
iii. Patient has lost ≥ 5% of baseline body weight.

2. Weight Loss in Adolescents Aged ≥ 12 to < 18 Years. Note: For individuals who have not completed the initial 3 months of therapy, criterion 2, A must be met (do not use continuation criteria if the initial 3 months were not completed).

A) Initial Therapy. Approve for 3 months if the patient meets the following criteria (i, ii, and iii):
i. Patient 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 severe co-morbidity (type 2 diabetes mellitus, premature cardiovascular disease) or has a strong family history of type 2 diabetes or premature cardiovascular disease (CVD); AND
ii. Patient 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 co-morbidities; AND
iii. Patient is currently engaged in behavioral modification and on a reduced calorie diet.

B) Patients Continuing Therapy. Approve for 12 months if the patient meets the following criteria (i, ii, iii and iv):
i. Patient 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 severe co-morbidity (type 2 diabetes or premature CVD) or strong family history of type 2 diabetes or premature CVD; AND
ii. Patient is currently engaged in behavioral modification and on a reduced calorie diet; AND
iii. Patient's current BMI percentile has decreased for age and weight (taking into account that the patient is increasing in height and will have a different normative BMI from when Xenical was started); AND
iv. Patient currently has a BMI > 85th percentile.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

These drugs for weight loss have not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

1. Combination Appetite Suppressant Therapy. Appetite suppressants (benzphetamine, diethylpropion, phendimetrazine tartrate, phentermine hydrochloride or resin, Belviq, Qsymia, Contrave, Saxenda) are indicated *only* as monotherapy and should not be used in combination with other appetite suppressant drugs.[5-11,28-29,32,33] A 12-week randomized trial compared safety and efficacy of Belviq monotherapy vs. Belviq plus phentermine (either once daily or twice daily).[34] Although addition of phentermine resulted in increased weight loss, patients on Belviq plus phentermine twice-daily had higher dropout rates due to adverse events (11.4% vs. 5.1% with Belviq monotherapy). The study was of inadequate size and duration to assess for long-term safety, particularly in regard to cardiovascular outcomes.

2. **Simultaneous Use of Xenical with Any of the Following: benzphetamine, diethylpropion, phendimetrazine tartrate, or phentermine hydrochloride or resin, Belviq, Belviq XR, Contrave, Saxenda or Qsymia.** Limited information from published well-controlled studies is available on the combination use of these drugs. Using weight loss drugs one at a time and starting with the lowest effective doses can decrease the chance of adverse effects.[2] Unproven combination therapy is not recommended.[4]

3. **Treatment of Hyperlipidemia in Non-Obese Patients**. Short-term use of Xenical has slightly decreased total and low density lipoprotein (LDL) cholesterol in patients with increased total and LDL cholesterol levels and normal triglyceride levels who were not obese (BMI 19 to 28.7 kg/m^2).[22] Triglycerides were unchanged and high density lipoprotein (HDL) cholesterol tended to decrease. Although not directly compared with other drugs, Xenical's effects on total and LDL cholesterol were less than those observed with hydroxy-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (HMGs) and low dose cholestyramine.

4. **Treatment of Binge-Eating Disorder in Non-Obese Patients (BMI < 30 kg/m^2 or < 27 kg/m^2 for Those with Risk Factors).** In a short term (12 or 24 week) placebo-controlled trial in obese patients (BMI ≥ 30 kg/m^2) with binge eating disorder, Xenical has been effective in producing weight loss.[23-24] Patients with binge-eating disorder are usually obese and should be reviewed for weight loss therapy using the criteria for Xenical in the section above.

5. **Prevention of Diabetes in Patients with BMI < 30 kg/m^2.** In a large (n = 3,305) 4-year study, Xenical, in addition to lifestyle changes, led to a 37% risk reduction in the development of type 2 diabetes in obese (BMI ≥ 30 kg/m^2) patients compared with placebo.[19] However, those most affected had impaired glucose tolerance at baseline and these patients achieved a more pronounced weight reduction. Qsymia in addition to lifestyle modification reduced the progression to type 2 diabetes in overweight/obese patients (BMI 27 to 45 kg/m^2) plus at least two weight-related comorbidities with pre-existing prediabetes and/or metabolic syndrome in a 108-week study compared with placebo (n = 475). However, the magnitude of effect for prevention of type 2 diabetes was related to the degree of weight loss achieved in this sub-analysis. Similar findings were seen with Belviq in CAMELLIA-TIMI 61 (n = 12,000), a study of overweight or obese patients (BMI ≥ 27 kg/m^2) with diabetes, prediabetes, and normoglycemia.[36] Belviq plus lifestyle modifications reduced glycosolated hemoglobin (HbA_{1C}) by 0.33% versus placebo in diabetic patients and decreased risk of incident diabetes by 19% and 23% in prediabetic and normoglycemic patients, respectively. Statistically significant weight loss beyond placebo of 2.6 kg, 2.8 kg, and 3.3 kg was achieved for diabetic, prediabetic, and normoglycemic patients, respectively. Like with Qysmia, the glycemic benefit is believed to be primarily attributed to weight loss.[37] Such patients should be evaluated based on overweight or obesity using the appropriate criteria above.

6. **Nonalcoholic Fatty Liver Disease.** In a single-center trial, 52 patients with nonalcoholic fatty liver disease were randomized to Xenical 120 mg three times daily or placebo.[25] Mean BMI was 33 kg/m^2. All patients were in a behavioral weight loss program. Forty-four patients completed 6 months and their results were analyzed. Patients were not well-matched for baseline characteristics (e.g., BMI, waist circumference, glucose and insulin levels were significantly different between groups at baseline). The authors concluded that Xenical improves serum alanine aminotransferase (ALT) and steatosis on ultrasound in these patients beyond its effect on weight reduction. Long-term, well-designed trials in a large number of patients are needed to determine if Xenical has a place in therapy for nonalcoholic fatty liver disease. There is very little good quality evidence to support or refute the use of weight reduction as a treatment for nonalcoholic fatty liver disease.[26]

7. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Selected revision	Criteria for Saxenda added to policy.	04/15/2015
Annual revision	No criteria changes.	10/21/2015
DEU revision	Generics Regimex 25 mg tracked into the Weight Loss Drugs PA rule.	04/27/2016
Annual revision	Belviq XR added to policy (same criteria as Belviq). Bontril SR removed from the policy (obsolete for > 3 years). Lomaira added to policy.	10/19/2016
Annual revision	No criteria changes.	10/18/2017
Annual revision	Brand Didrex® removed from policy (obsolete for > 3 years). **Prevention of Diabetes in Patients with BMI < 30 kg/m^2:** Indication title reworded for clarity. The following were removed from Conditions Not Recommended for Approval as this information is captured within criteria: • **Benzphetamine, diethylpropion, phendimetrazine and phentermine (hydrochloride or resin) in Children or Adolescents ≤ 16 Years of Age** • **Belviq, Belviq XR, Contrave, Saxenda, and Qsymia in Patients < 18 Years of Age** • **Xenical in Children < 12 Years of Age**	10/24/2018

TAC – Therapeutic Assessment Committee; DEU – Drug Evaluation Unit; * For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx.

APPENDIX A

Below is a chart of BMI based on various heights and weights.[2] To use the table, find the appropriate height in the far left column, and move across the row to the given weight; the number at the top of the column is the BMI. For example, a patient who is 5 feet 6 inches in height and weighs 192 pounds has a BMI of 31 kg/m^2.

BMI can also be calculated using the following formula: BMI equals body weight in kilograms divided by height meters squared (m^2), i.e., BMI = kg/m^2.

BODY MASS INDEX

BMI, kg/m^2	**25**	**26**	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**	**40**
Height (feet, inches)	**Weight (pounds)**											
4'10"	119	124	129	134	138	143	148	153	158	162	167	191
4'11"	124	128	133	138	143	148	153	158	163	168	173	198
5'0"	128	133	138	143	148	153	158	163	168	174	179	204
5'1"	132	137	143	148	153	158	164	169	174	180	185	211
5'2"	136	142	147	153	158	164	169	175	180	186	191	218
5'3"	141	146	152	158	163	169	175	180	186	191	197	225
5'4"	145	151	157	163	169	174	180	186	192	197	204	232
5'5"	150	156	162	168	174	180	186	192	198	204	210	240
5'6"	155	161	167	173	179	186	192	198	204	210	216	247
5'7"	159	166	172	178	185	191	198	204	211	217	223	255
5'8"	164	171	177	184	190	197	203	210	216	223	230	262
5'9"	169	176	182	189	196	203	209	216	223	230	236	270
5'10"	174	181	188	195	202	209	216	222	229	236	243	278
5'11"	179	186	193	200	208	215	222	229	236	243	250	286
6'0"	184	191	199	206	213	221	228	235	242	250	258	294
6'1"	189	197	204	212	219	227	235	242	250	257	265	302
6'2"	194	202	210	218	225	233	241	249	256	264	272	311
6'3"	200	208	216	224	232	240	248	256	264	272	279	319
6"4"	205	213	221	230	238	246	254	263	271	279	287	328