

MTF Formulary Management for Weight Loss Agents

Defense Health Agency Pharmacy Operations Division

Bottom Line

- NDAA 2017 authorizes coverage of weight loss drugs under the TRICARE Pharmacy benefit at the MTFs, TRICARE Mail Order and Retail Network pharmacies.
- Only the generic products (phentermine, benzphetamine, diethylpropion and phendimetrazine) were designated as Uniform Formulary. The branded products Saxenda, Belviq/Belviq XR, Contrave, Xenical, and Lomaira are all non formulary.
- No weight loss agent was selected for addition to the Basic Core Formulary (BCF).
- All the weight loss agents require manual prior authorization – patients must try behavioral modification first. Additionally, a trial of a generic product is also required prior to the branded non formulary products. See below.
- Active Duty Service Members requiring a weight loss drug should be enrolled in a Service-Specific Health and Wellness Program and must follow individual service policies.
- Overall, these drugs have a modest effect on weight loss, and evidence for sustained weight loss beyond two years is minimal. Clinical comparisons between the individual drugs are difficult, due to differences in the mechanisms of action, lack of head-to-head trials between products, lack of cardiovascular outcomes trials and differing side effect profiles.
- The projected budget impact of TRICARE coverage for the weight loss drugs is unknown at this time, but could range from \$10 Million to \$100 Million annually, which is why Prior Authorization is required.

Uniform Formulary Decision: The Director, DHA, approved the recommendations from the November 2017 DoD P&T Committee meeting on January 31, 2018. Implementation will occur by May 2, 2018.

BCF drugs MTFs <u>must</u> have on formulary	Uniform Formulary MTFs <u>may</u> have on formulary	Nonformulary MTFs <u>must not</u> have on formulary
<ul style="list-style-type: none"> • None 	<ul style="list-style-type: none"> • phentermine (Adipex-P generics) • benzphetamine (Didrex generics) • diethylpropion (Tenuate generics) • phendimetrazine IR and SR (Bontril, Bontril SR generics) 	<ul style="list-style-type: none"> • liraglutide (Saxenda) • lorcaserin IR/ER (Belviq, Belviq XR) • naltrexone SR/bupropion SR (Contrave) • orlistat (Xenical) • phentermine/topiramate ER (Qsymia) • phentermine 8 mg (Lomaira)

Background

- Prior to NDAA 2017, weight loss agents were excluded from the pharmacy benefit. However, an Interim Final Rule published on September 29, 2017 (DOD-2017-HA-RIN 0720) authorizes coverage for weight loss agents under TRICARE Prime and TRICARE Select for medically necessary treatment of obesity.
- Professional treatment guidelines from several organizations differ with respect to recommendations for weight loss. **However, all the guidelines agree that comprehensive lifestyle intervention is the foundation of weight loss treatment and should be included as part of any weight loss program.** Pharmacotherapy may be offered to patients with a body mass index (BMI) ≥ 30 and to those with a BMI ≥ 27 who have obesity-associated comorbidities.
- The older generic drugs (diethylpropion, phentermine, benzphetamine, and phendimetrazine) and Lomaira are approved for short-term (≤ 12 weeks) treatment of obesity. The newer branded products Saxenda, Belviq, Belviq XR, Xenical, Qsymia, and Contrave are approved for long-term treatment of obesity (>12 weeks).
- Weight loss is a surrogate for decreased cardiovascular risk. However, there are no long-term cardiovascular outcome studies available that demonstrate reduced cardiovascular risk with continuous use of the weight loss drugs.

- Common adverse reactions for most agents include increased heart rate, nausea, and diarrhea. Discontinuations due to adverse events can be of concern. All of these drugs are contraindicated in pregnancy (Category X).

Efficacy

- The majority of FDA-approved weight loss agents were studied in placebo controlled trials, and vary significantly in their reported efficacy and safety. The individual trials also varied in the requirements for concurrent lifestyle interventions, including exercise and dietary modification.
- A 2015 systematic review from the Institute for Clinical & Economic Review (ICER) evaluated 17 placebo-controlled trials with Belviq, Contrave, Qsymia, and Saxenda. Qsymia and Saxenda had the highest proportion of patients achieving a >5% weight loss (75% and 73%, respectively), compared to 52% with Contrave and 44% with Belviq.
 - Discontinuations due to adverse drug reactions (ADRs) occurred most commonly with Qsymia (1.3-16%) and Contrave (19-29%).
- A 2016 systematic review in the Journal of the American Medical Association (JAMA) included 28 studies with Belviq, Contrave, Qsymia, Saxenda, and Xenical. Qsymia and Saxenda had the highest odds of achieving a 5% weight loss from baseline, followed by Contrave. Saxenda and Contrave had the highest discontinuation rate from adverse events.
- Discontinuation of any weight loss agent is associated with weight regain, however, differences in study design make direct comparisons difficult regarding weight regain.

Weight Loss Products

Phentermine/topiramate ER (Qsymia)

- The fixed-dose combination of phentermine/topiramate ER (Qsymia) is dosed once daily and is a controlled substance (C-IV). Its mechanism in reducing weight is to suppress appetite.
- **The topiramate ER component of Qsymia contains different mg strengths than generic topiramate IR. However, generic phentermine and generic topiramate IR (off-label use) can be administered concomitantly for weight loss. Generic topiramate IR does not require prior authorization, in contrast to topiramate ER.**
- Qsymia is the only weight loss drug that showed a clinically significant reduction in blood pressure, and a significant reduction in patient progression to type 2 diabetes.
- Qsymia requires a REMS due to safety concerns in pregnant women and risk of congenital malformations. Patients with hypertension, elevated heart rate, or renal dysfunction should use Qsymia with caution.

Liraglutide (Saxenda)

- Liraglutide (Saxenda) is a glucagon-like peptide-1 receptor agonist (GLP-1RA) administered 3 mg subcutaneously once daily. It causes weight loss by increasing satiety. Saxenda has been shown to reduce hemoglobin A1c in type 2 diabetics.
- Liraglutide is also available in a 1.8 mg formulation labeled for treating diabetes under the tradename Victoza. In a two-year dose comparison study, liraglutide 1.8 mg displayed comparable efficacy to Saxenda 3mg in weight loss.
- Other GLP1RAs, including exenatide once weekly (Bydureon), cause weight loss. In the 26-week DURATION-6 trial, Bydureon reduced baseline weight by 2.7 kg in patients with type 2 diabetes compared to 3.6 kg with Victoza, a statistically significant but not clinically relevant difference. **Patients requiring a GLP1RA for treatment of diabetes should receive one of the step-preferred GLP1RA products, and not Saxenda.**
- **Saxenda is the least cost-effective weight loss drug.**
- Labeling for Saxenda includes a boxed warning for thyroid C-cell tumors in mice, however this effect has not been confirmed in humans.

Naltrexone SR/bupropion (Contrave)

- The fixed dose combination of naltrexone SR/bupropion (Contrave) is dosed twice daily and reduces cravings. The individual components of bupropion SR and naltrexone are used off-label for obesity.

- Contrave demonstrated a decrease in A1c of 0.6% from baseline compared to 0.1% with placebo in one study of patients with type 2 diabetes.
- Contrave labeling has a black box warning against use in major depression or psychiatric disorders, and should be avoided in patients who have a history of seizures, uncontrolled hypertension, and in patients taking opioids.

Orlistat (Xenical)

- Orlistat (Xenical) is a lipase inhibitor given three times daily with high fat meals. It is the only product approved for treating pediatric patients as young as 12 years.
- Xenical should be avoided in patients with gallbladder disease or malabsorption syndromes.

Lorcaserin (Belviq/ Belviq XR)

- Lorcaserin (Belviq) is given once (XR) or twice daily (IR) and is a controlled substance (C-IV). The mechanism by which lorcaserin induces weight loss is unknown.
- In a trial enrolling patients with type 2 diabetes, Belviq decreased A1c by 0.9% compared to 0.4% with placebo.
- Belviq should be used with caution when administered with other serotonergic agents due to the risk of serotonin syndrome. Patients with congestive heart failure, bradycardia, heart valve problems, and patients with second or third degree heart block require close monitoring.

Phentermine 8 mg (Lomaira)

- Phentermine 8 mg (Lomaira) is a branded product that contains a lower dose of phentermine than that found in the generic products (15 mg, 37.5 mg).
- Lomaira is non formulary, and much more costly than generic phentermine. Reserve use only for patients experiencing elevated baseline heart rates with generic phentermine doses of 15 mg. The same cardiovascular precautions that apply to the 15 mg and 37.5 mg phentermine products also apply to Lomaira.

Prior Authorization (PA)

- All new and current users of the weight loss agents (including the generic drugs and branded products) must complete a manual PA.
- **For all the products, lifestyle intervention is required for 6 months prior to starting therapy, and must be continued throughout therapy. Additionally, a trial of a generic product is also required prior to the branded non formulary products.**
- The PA criteria take into account the individual safety profiles for the different drugs. PA is not approved for patients who are pregnant.
- **Patients with a prescription for Saxenda must try the generic products and Qsymia, Contrave, Belviq/Belviq XR and Xenical first.**
- **Adult patients with a prescription for Xenical must try the generic products and Qsymia, Contrave, and Belviq/Belviq XR first.**
- Pediatric patients between the ages of 12 to 17 years requiring Xenical must also undergo PA.
- **Off-label uses (e.g., for non-alcoholic steatohepatitis [NASH]) are not approved.**
- **The general PA criteria applying to branded weight loss agents are listed below.** For the full manual PA criteria, refer to the November 2017 DoD P&T Committee meeting minutes, or the PA forms found on the TRICARE Formulary Search Tool (forms will be available May 2nd). See links provided below.
 1. Age \geq 18 (unless the request is for Xenical in an adolescent)
 2. The patient has tried and failed to achieve a 5% reduction in baseline weight after a 12 week course of phentermine unless there is a history of cardiovascular disease (e.g. arrhythmias, coronary artery disease, heart failure, stroke, uncontrolled hypertension), hyperthyroidism, or significant contraindication to phentermine.

3. The patient has a BMI \geq 30, or a BMI \geq 27 for those with one of the following comorbidities: diabetes, impaired glucose tolerance, dyslipidemia, hypertension, sleep apnea.
4. The patient has engaged in a trial of behavioral modification and dietary restriction for at least 6 months and will remain engaged throughout course of therapy.
5. The patient is not pregnant.
6. FOR Active Duty Service Members: Individuals must be enrolled in a Service-specific Health/Wellness Program AND adhere to Service policy, AND will remain engaged throughout course of therapy.
7. For the generic products and Lomaira, PA will expire after 3 months; for the branded products PA will expire in 4 months. Renewal will be allowed for an additional 12 months if the patient has lost at least 5% of baseline body weight since starting therapy and continues to engage in lifestyle modification.

References

- Systematic Review and Meta-analysis. JAMA 2016;315(22):2424-34.
- Obesity Management Final Report ICER 2015: <https://icer-review.org/material/obesity-management-final-report/>
- DoD P&T Committee minutes: <http://health.mil/PandT>
- Current/future drug classes under review by the DoD P&T Committee: <http://www.health.mil/About-MHS/Other-MHS-Organizations/DoD-Pharmacy-and-Therapeutics-Committee>
- TRICARE Formulary Search Tool: <http://www.health.mil/formulary>
- Prior Authorization/Medical Necessity forms: See Formulary Search Tool above.
- Formulary Management Documents (including this one) available at: <http://www.health.mil/DoDPTResources>
- Point of contact for additional information: dha.jbsa.pharmacy.list.poduf@mail.mil

Weight Loss Agents Price Comparison at MTF	
Drug	MTF Cost/Month (Nov 2017)
Uniform Formulary	
<ul style="list-style-type: none"> • phentermine • benzphetamine • diethylpropion • phendimetrazine 	\$ Most Cost Effective
Non-Formulary	
<ul style="list-style-type: none"> • lorcaserin (Belviq/Belviq XR) • naltrexone/bupropion SR (Contrave) • phentermine/topiramate ER (Qsymia) • phentermine (Lomaira) 	\$\$\$ Less Cost-Effective
<ul style="list-style-type: none"> • orlistat (Xenical) • liraglutide (Saxenda) 	\$\$\$\$ Least Cost-Effective
Legend: \$ = "Most Cost-Effective" represents Rx's with the <u>lowest cost</u> and best clinical efficacy \$\$ = "Less Cost-Effective" represents <u>higher cost</u> Rx's with similar clinical efficacy \$\$\$ = "Less Cost-Effective" represents <u>next higher cost</u> Rx's with similar clinical efficacy \$\$\$\$ = "Least Cost-Effective" represents Rx's with the <u>highest cost</u> with similar clinical efficacy	