Weight Management
### Body Mass Index (BMI) classifications

<table>
<thead>
<tr>
<th>Classification</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt;18.5</td>
</tr>
<tr>
<td>Normal</td>
<td>18.5–24.9</td>
</tr>
<tr>
<td>Overweight</td>
<td>25.0–29.9</td>
</tr>
<tr>
<td>Obese I</td>
<td>30.0–34.9</td>
</tr>
<tr>
<td>Obese II</td>
<td>35.0–39.9</td>
</tr>
<tr>
<td>Obese III</td>
<td>≥40</td>
</tr>
</tbody>
</table>

Disease risk for obesity-associated chronic health conditions is directly correlated with increasing BMI and waist circumference.

Gender-specific cutoffs for increased waist circumference:
- **Men**: >40 inches (102 centimeters)
- **Women**: >35 inches (88 centimeters)
Select medications associated with weight gain*1-5

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticonvulsants</td>
<td>Carbamazepine, valproic acid, pregabalin, gabapentin</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Amitriptyline, mirtazapine, paroxetine</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>Clozapine, olanzapine, quetiapine, risperidone, thioridazine</td>
</tr>
</tbody>
</table>
| Antidiabetic agents | • Insulin  
|                   | • **Meglitinides**: nateglinide, repaglinide                                  |
|                   | • **Sulfonylureas**: chlorpropamide, glimepiride, glipizide                  |
|                   | • **Thiazolidinediones**: pioglitazone, rosiglitazone                         |
| Beta-blockers     | Atenolol, metoprolol, propranolol                                           |
| Glucocorticoids   | Prednisone                                                                  |
| Contraceptives    | Medroxyprogesterone acetate depot injection                                  |
| Mood stabilizers  | Lithium                                                                     |

*Please refer to VA/DoD Clinical Practice Guideline For The Management of Adult Overweight and Obesity for more information.
<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>LEVEL 1</th>
<th>LEVEL 2</th>
<th>LEVEL 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥25 with obesity-associated condition(s)†</td>
<td>Comprehensive lifestyle intervention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥27 with obesity-associated condition(s)† OR ≥30</td>
<td>Comprehensive lifestyle intervention</td>
<td>Consider drug therapy</td>
<td></td>
</tr>
<tr>
<td>≥35 with obesity-associated condition(s)† OR ≥40</td>
<td>Comprehensive lifestyle intervention</td>
<td>Consider drug therapy</td>
<td>Consider surgery</td>
</tr>
</tbody>
</table>

†Obesity-associated conditions: see table at right

### Common obesity-associated conditions*

#### The following conditions are directly influenced by weight:
- Degenerative joint disease
- Dyslipidemia**
- Hypertension**
- Metabolic syndrome
- Non-alcoholic fatty liver disease (NAFLD)
- Obstructive sleep apnea
- Type 2 diabetes and pre-diabetes**

*Increased waist circumference is considered an obesity comorbidity equivalent;
**At least moderate evidence exists for modifying these conditions with weight loss\(^6\)\(^8\)
Examples of aerobic physical activities and intensities

**Moderate intensity**
- Walking briskly (three miles per hour or faster, but not race-walking)
- Water aerobics
- Bicycling slower than 10 miles per hour
- Tennis (doubles)
- Ballroom dancing
- General gardening

**Vigorous intensity**
- Racewalking, jogging, or running
- Swimming laps
- Tennis (singles)
- Aerobic dancing
- Bicycling 10 miles per hour or faster
- Jumping rope
- Heavy gardening (continuous digging or hoeing, with heart rate increase)
- Hiking uphill or with a heavy backpack
Healthy diet

A healthy diet is one of the three pillars of comprehensive lifestyle intervention.

- Dietary restrictions and physical activity should result in a total calorie deficit of 500 to 1,000 kcal/day to achieve weight loss of one to two pounds/week for the first 12 to 16 weeks.
- From the standpoint of creating a calorie deficit, the choice of a specific diet is less important; rather it is the attainment of caloric deficit that is the key to weight loss.\footnote{10}
- Any nutritionally balanced diet can be recommended (see examples in table below).

<table>
<thead>
<tr>
<th>Diet approach</th>
<th>Content (% of total calories)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Fat</td>
</tr>
<tr>
<td>Very low carbohydrates (high-fat)</td>
<td>55-65</td>
</tr>
<tr>
<td>Low carbohydrates (moderate-fat)</td>
<td>20-30</td>
</tr>
<tr>
<td>Moderate-fat, balanced nutrient reduction (low-calorie)</td>
<td>20-30</td>
</tr>
<tr>
<td>Low-fat</td>
<td>11-19</td>
</tr>
</tbody>
</table>
Pharmacotherapy’s place in therapy*

- **Weight Management Medications (WMM)** should be offered to patients with a body mass index (BMI) ≥30 kg/m² and to those with a BMI ≥27 kg/m² who also have obesity-associated conditions as an adjunct to comprehensive lifestyle intervention, or when comprehensive lifestyle intervention alone does not produce the desired weight loss.

- WMM can be initiated anytime during participation in a clinically supported weight management program.

- If sufficient weight loss is not achieved after 12-16 weeks of pharmacotherapy or significant weight regain occurs, the WMM should be discontinued (See individual Criteria for Use for details). A trial of a different WMM may be warranted provided the patient is compliant with comprehensive lifestyle interventions.

*Refer to PBM criteria for use.
Common to all the criteria for use of WMM are the following:**

**Exclusion criteria**

1. Pregnancy
2. The patient is taking another weight loss medication concurrently.

**Inclusion criteria**

- The patient is participating in a clinically supported weight management program that targets all three aspects of weight management (i.e., diet, physical activity, behavioral changes).
- The patient’s medication regimen has been reviewed to identify and discontinue medications associated with weight gain when clinically safe and appropriate.

The patient’s BMI is $\geq 30 \text{ kg/m}^2$ OR

The patient’s BMI is $\geq 27 \text{ kg/m}^2$ with at least one weight-related comorbidity such as hypertension, type 2 diabetes mellitus, dyslipidemia, metabolic syndrome, obstructive sleep apnea, or degenerative joint disease (osteoarthritis).

**Each WMM CFU has additional exclusion and inclusion criteria pertaining to its particular safety profile.**
### General considerations in selection of pharmacotherapy

<table>
<thead>
<tr>
<th>Weight management medication</th>
<th>REMS*</th>
<th>Controlled substance schedule</th>
<th>Boxed warning</th>
<th>Route of administration</th>
<th>Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine/topiramate ER (Qsymia®)</td>
<td>Yes**</td>
<td>CIV</td>
<td>No</td>
<td>Oral</td>
<td>Once daily (initial dose titration)</td>
</tr>
<tr>
<td>Naltrexone/bupropion ER (Contrave®)</td>
<td>No</td>
<td>None</td>
<td>Yes (suicidal thoughts/behaviors)</td>
<td>Oral</td>
<td>Titration to twice daily</td>
</tr>
<tr>
<td>Orlistat (Xenical®, Alli®)</td>
<td>No</td>
<td>None</td>
<td>No</td>
<td>Oral</td>
<td>Three times daily</td>
</tr>
<tr>
<td>Liraglutide (Saxenda®)</td>
<td>No</td>
<td>None</td>
<td>Yes (thyroid C-cell tumors)</td>
<td>Injection (SC)</td>
<td>Once daily (initial dose titration)</td>
</tr>
</tbody>
</table>

Criteria for use of the individual agents for chronic weight management are available in VA PBM Criteria for Use. VA Formulary information at: www.pbm.va.gov/apps/VANationalFormulary

**ER:** extended-release; **SC:** subcutaneous; **XR:** extended release

*REMS: Risk Evaluation and Mitigation Strategy; **REMS:** Phentermine/topiramate ER—to prevent unintended exposure during pregnancy, as topiramate is associated with oral clefts in newborns exposed during the first trimester; requirements for provider and pharmacy certification
## Phentermine/topiramate ER (Qsymia®)

### Dosing

- Phentermine 3.75 mg/topiramate 23 mg extended-release capsule each morning for 14 days; then increase to 7.5 mg/46 mg each morning for an additional 12 weeks
- If a weight loss of 3% of baseline body weight is not achieved after 12 weeks, then increase the dose to 11.25 mg/69 mg each morning for 14 days; then increase to 15 mg/92 mg (maximum dose) daily

### Dose adjustments (if applicable)

**Dose in renal impairment:**
- Moderate-severe renal impairment (CrCl <50 mL/min): should not exceed 7.5 mg/46 mg once daily

**Dose in hepatic impairment:**
- Moderate hepatic impairment (Child-Pugh score 7-9) should not exceed 7.5 mg/46 mg once daily

### Monitoring

- Weight
- Blood pressure (orthostatic) and/or signs/symptoms of hypotension
- Resting heart rate
- Serum bicarbonate, especially if patient is taking another carbonic anhydrase inhibitor
- Serum potassium, especially if patient is taking another carbonic anhydrase inhibitor
- Glucose and/or signs/symptoms of hypoglycemia in patients with diabetes
- Mood (depression) and sleep disorders
- Pregnancy tests in women of reproductive age

### Common side effects

- Increased heart rate
- Paresthesia
- Dizziness
- Dysgeusia
- Headache
- Insomnia
- Decreased serum bicarbonate
- Xerostomia
- Constipation

### Contraindications

- Pregnancy
- Glaucoma
- Hyperthyroidism
- MAOI use during or within 14 days

### Warnings

- Pregnancy
- Glaucoma
- Hyperthyroidism
- MAOI use during or within 14 days

- Metabolic acidosis
- Cognitive impairment
- Elevated heart rate
- Nephrolithiasis
- Hypokalemia
- Mood and sleep disorders
- Depression or suicidal ideation
- Increased creatinine
- Adjust hypoglycemic medications to avoid hypoglycemia
# Naltrexone/bupropion ER (Contrave®)

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Dose adjustments (if applicable)</th>
<th>Monitoring</th>
<th>Common side effects</th>
<th>Contraindications</th>
<th>Warnings</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Naltrexone 8 mg/bupropion 90 mg tablet dose escalation schedule:</td>
<td><strong>Morning</strong></td>
<td><strong>Weight</strong></td>
<td><strong>Headache</strong></td>
<td><strong>Opioid use (agonists or partial agonists)</strong></td>
<td>• Suicidal thinking/behavior [U.S. Boxed Warning]</td>
</tr>
<tr>
<td></td>
<td><strong>Evening</strong></td>
<td><strong>Pregnancy tests in women of child-bearing potential as deemed necessary</strong></td>
<td><strong>Sleep disorder</strong></td>
<td><strong>Pregnancy</strong></td>
<td>• Neuropsychiatric symptoms</td>
</tr>
<tr>
<td></td>
<td><strong>Week 1:</strong> 1 tablet None</td>
<td><strong>Glucose and/or signs/symptoms of hypoglycemia in patients with diabetes (as adjustment in a patient’s diabetes medication may be needed to avoid hypoglycemia)</strong></td>
<td><strong>Nausea</strong></td>
<td><strong>Uncontrolled hypertension</strong></td>
<td>• May precipitate acute opioid withdrawal in patients receiving opioids</td>
</tr>
<tr>
<td></td>
<td><strong>Week 2:</strong> 1 tablet 1 tablet</td>
<td><strong>Blood pressure and/or signs/symptoms of hyper- or hypotension</strong></td>
<td><strong>Constipation</strong></td>
<td><strong>Seizure disorder</strong></td>
<td>• Seizures</td>
</tr>
<tr>
<td></td>
<td><strong>Week 3:</strong> 2 tablets 1 tablet</td>
<td><strong>Heart rate</strong></td>
<td><strong>Diarrhea</strong></td>
<td><strong>Bulimia or anorexia nervosa</strong></td>
<td>• Increase blood pressure, heart rate</td>
</tr>
<tr>
<td></td>
<td><strong>Week ≥4:</strong> 2 tablets 2 tablets</td>
<td><strong>Signs and symptoms of depression, suicidal thoughts or behavior, cognitive impairment, or changes in mood</strong></td>
<td><strong>Vomiting</strong></td>
<td><strong>Acutely discontinuation of alcohol</strong></td>
<td>• Hepatotoxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Dizziness</strong></td>
<td><strong>Dizziness</strong></td>
<td><strong>Concomitant MAOI use or initiation in patients receiving linezolid or IV methylene blue</strong></td>
<td>• Adjust hypoglycemic medications to avoid hypoglycemia</td>
</tr>
<tr>
<td></td>
<td><strong>Dose in renal impairment:</strong></td>
<td><strong>Xerostomia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Moderate or severe renal impairment: maximum recommended daily dose is one tablet each morning and evening</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Not recommended for use in patients with end-stage renal disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Dose in hepatic impairment:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Maximum recommended daily dose of naltrexone/bupropion is one tablet in the morning</td>
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<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>
### Orlistat (Xenical®, Alli®)

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Dose adjustments (if applicable)</th>
<th>Monitoring</th>
<th>Common side effects⁷</th>
<th>Contraindications⁷</th>
<th>Warnings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Xenical®:</strong> 120 mg 3 times daily with each main meal containing fat (during or up to one hour after the meal); omit dose if meal is occasionally missed or contains no fat</td>
<td>There are no dosage adjustments provided in the manufacturer's labeling</td>
<td>Weight</td>
<td>Gastrointestinal effects (e.g., oily rectal leakage, abdominal distress/pain, flatulence with discharge, bowel urgency, steatorrhea) —typically frequency decreases over time</td>
<td>Pregnancy</td>
<td>Increased urinary oxalate and nephrolithiasis</td>
</tr>
<tr>
<td><strong>Alli®:</strong> OTC labeling: 60 mg 3 times daily with each main meal containing fat</td>
<td></td>
<td>Blood pressure (orthostatic) and/or signs/symptoms of hypotension</td>
<td></td>
<td>Chronic malabsorption syndrome</td>
<td>Hepatotoxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Glucose and/or signs/symptoms of hypoglycemia in patients with diabetes</td>
<td></td>
<td>Cholelithiasis</td>
<td>Cholelithiasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Liver function tests if signs or symptoms of hepatic dysfunction</td>
<td></td>
<td></td>
<td>Interference with absorption of fat-soluble vitamins, cyclosporine, thyroid hormone, and anti-convulsants</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Adjust hypoglycemic medications to avoid hypoglycemia</td>
</tr>
</tbody>
</table>
Liraglutide (Saxenda®)

<table>
<thead>
<tr>
<th>Dosing</th>
<th>Dose adjustments (if applicable)</th>
<th>Monitoring</th>
<th>Common side effects</th>
<th>Contraindications</th>
<th>Warnings</th>
</tr>
</thead>
</table>
| **Initiate dose titration with 0.6 mg injected subcutaneously daily for one week; increase the daily dose by 0.6 mg per week until reaching the target dose of 3 mg. Slow titration rate to every other week if the patient does not tolerate weekly dose escalation** | **In patients on secretagogues (such as sulfonylureas) or insulin:**  
  - Consider reducing the dose of the secretagogue or insulin by 50% to reduce the risk of hypoglycemia and monitor blood glucose when initiating liraglutide | **Weight**  
**Blood pressure (orthostatic) and/or signs/symptoms of hypotension**  
**Resting heart rate**  
**Glucose and/or signs/symptoms of hypoglycemia**  
**Mood (symptoms of depression) and sleep disorders** | **Increased heart rate**  
**Headache**  
**Hypoglycemia**  
**Nausea**  
**Diarrhea**  
**Constipation**  
**Vomiting**  
**Dyspepsia**  
**Abdominal pain**  
**Fatigue** | **Pregnancy**  
**Personal or family history of medullary thyroid carcinoma [U.S. Boxed Warning] or multiple endocrine neoplasia type 2 (MEN2)** | **Injection site reactions**  
**Hypersensitivity reactions; use caution in patients with history of reaction to glucagon-like peptide-1 receptor agonists**  
**Pancreatitis**  
**Acute cholelithiasis and cholecystitis**  
**Tachycardia**  
**Acute renal failure and chronic renal failure exacerbation**  
**Suicidal behavior and ideation**  
**Adjust hypoglycemic medications to avoid hypoglycemia** |
| **Discontinue if 4% weight loss is not achieved by week 16 as it is unlikely that a meaningful weight loss will be achieved and sustained with continued treatment** | **Dose in renal impairment:**  
- Use with caution in renal impairment | | | | |
## Common drug interactions

<table>
<thead>
<tr>
<th>Weight management medication</th>
<th>Interacting medication</th>
</tr>
</thead>
</table>
| Phentermine/topiramate ER    | • Monoamine oxidase inhibitors (discontinue ≥14 days before initiating phentermine/topiramate)  
|                              | • Sympathomimetic amines                                                                |
|                              | • Concurrent phentermine or topiramate                                                  |
| Naltrexone/bupropion ER      | • Monoamine oxidase inhibitors (discontinue ≥14 days before initiating naltrexone/bupropion)  
|                              | • Opioid therapy                                                                        |
|                              | • Concurrent bupropion or naltrexone                                                    |
| Orlistat                     | • Antiepileptics (decreased effect)                                                    |
|                              | • Cyclosporine (decreased effect)                                                       |
|                              | • Levothyroxine (decreased effect)                                                      |
|                              | • Warfarin (enhanced effect)                                                            |
| Liraglutide                  | • Sulfonylureas and other hypoglycemic agents (hypoglycemia)                           |

**SSRI:** selective serotonin reuptake inhibitor; **SNRI:** serotonin norephinepherine reuptake inhibitor
Most common bariatric procedures$^{6,10,13-16}$

**Roux-en-Y Gastric Bypass$^{6,14-16}$**

- **Involves creation of 30 ml gastric pouch which empties into a roux limb of jejunum.** A variable distance downstream from this anastomosis, another anastomosis is created with the biliary limb to form a common channel which travels to the cecum.

- **Provides a restrictive component,** in that early satiety is produced with a small volume of food, with over-distention of the pouch resulting in nausea and vomiting, thus prompting dietary compliance.

- **Provides for a mal-absorptive component,** which is directly related to the length of the “common channel” of small intestine traveling to the cecum.

- Stimulates release of incretins and satiety gut peptides.

- Associated with iron deficient anemia, calcium, B12, folate, micronutrient vitamin and mineral deficiencies without appropriate supplementation. **Supplements are taken life-long following these procedures.**
Adjustable Gastric Banding\textsuperscript{6,14}

- **A silastic inflatable band is placed around the cardia of the stomach.** A reservoir port placed under the skin is subsequently injected with saline to expand or desufflate the band to create more or less restriction to food postoperatively.

- The adjustable gastric band may be considered a **reversible** form of the previously popular vertical banded gastroplasty.

- **Multiple post-operative band adjustments are often required.** The gastric band is a purely restrictive operation as there is no malabsorptive component.
Sleeve Gastrectomy$^{6,14,17}$

- Partial gastrectomy that can be performed laparoscopically in which most of the stomach is removed without bypassing the intestines (a type of restrictive operation).
- May provide further benefit through its effects on gut hormones (e.g., reduction in ghrelin) and is generally a safer procedure than Roux-en-Y gastric bypass.

Biliopancreatic Diversion or Duodenal Switch$^{14}$

- The duodenal switch procedure is similar to the biliopancreatic diversion except that the duodenum is capped and is bypassed along with the small bowel. Rather than create a pouch, the gastric remnant is a sleeve along the lesser curve and about four times the size of the gastric bypass pouch. Involves a partial gastrectomy that results in a 400 mL gastric pouch.
- The major advantage of these operations is that weight loss results irrespective of a patient’s eating habits.
- It retains the pylorus, minimizing problems related to dumping syndrome and marginal ulcer.
Important post-surgical considerations

1. Suicide risk
Suicide risk appears to be increased following bariatric surgery; increase vigilance for suicidal ideation and other risk factors for suicide (e.g., alcohol and other substance use disorder).

2. Nutritional Concerns
All patients should be followed and monitored routinely by an experienced team to detect nutritional deficiencies.
References


U.S. Department of Veterans Affairs

This reference guide was created to be used as a tool for VA providers and is available to use from the Academic Detailing SharePoint. These are general recommendations only; specific clinical decisions should be made by treating provider based on an individual patient’s clinical conditions.

VA PBM Academic Detailing Service Email Group:
PharmacyAcademicDetailingService@va.gov

VA PBM Academic Detailing Service SharePoint Site:
https://vaww.portal2.va.gov/sites/ad