

Weight Management A Quick Reference Guide for VA Clinicians (2019)



U.S. Department of Veterans Affairs

Veterans Health Administration PBM Academic Detailing Service





Weight Management

A Quick Reference Guide for VA Clinicians (2019)



U.S. Department of Veterans Affairs

Veterans Health Administration PBM Academic Detailing Service

Contents

Body Mass Index (BMI) classifications1
Specific medications associated with weight gain2
Weight loss interventions based on risk and BMI (kg/m ²)3
Examples of aerobic physical activities and intensities4
Healthy diet5
Pharmacotherapy's place in therapy
General considerations in selection of pharmacotherapy

Medication information for chronic weight management medications

Phentermine/topiramate ER (Qsymia [®])	9
Naltrexone/bupropion ER (Contrave®)	10
Orlistat (Xenical®, Alli®)	11
Liraglutide (Saxenda [®])	12
Common drug interactions	13
Most common bariatric procedures	14-16
Important post-surgical considerations	17
References	18-19

Body Mass Index (BMI) classifications

Classification	BMI (kg/m²)
Underweight	<18.5
Normal	18.5–24.9
Overweight	25.0–29.9
Obese I	30.0–34.9
Obese II	35.0–39.9
Obese III	≥40

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

Drug class	Medication
Anticonvulsants	Carbamazepine, valproic acid, pregabalin, gabapentin
Antidepressants	Amitriptyline, mirtazapine, paroxetine
Antipsychotics	Clozapine, olanzapine, quetiapine, risperidone, thioridazine
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.

Weight loss interventions based on risk and BMI (kg/m²)⁶

	LEVEL 1	LEVEL 2	LEVEL 3
BMI ≥25 with obesity- associated condition(s) ⁺	Comprehensive lifestyle intervention		
BMI ≥27 with obesity- associated condition(s) [†] OR BMI ≥30	Comprehensive lifestyle intervention	Consider drug therapy	
BMI ≥35 with obesity- associated condition(s) [†] OR BMI ≥40	Comprehensive lifestyle intervention	Consider drug therapy	Consider surgery

[†]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 loss⁵⁻⁸

Examples of aerobic physical activities and intensities⁹

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 diet⁶

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.¹⁰
- Any nutritionally balanced diet can be recommended (see examples in table below).

Diot approach	Content (% of total calories)				
	Fat	Carbohydrates	Protein		
Very low carbohydrates (high-fat)	55-65	<20 (<100g)	25-30		
Low carbohydrates (moderate-fat)	20-30	30-40	25-30		
Moderate-fat, balanced nutrient reduction (low-calorie)	20-30	55-60	15-20		
Low-fat	11-19	>65	10-20		



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.

**Each WMM CFU has additional exclusion and inclusion criteria pertaining to its particular safety profile.

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 ≥30 kg/m² OR The patient's BMI is ≥27 kg/m² 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).

General considerations in selection of pharmacotherapy

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

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

Medication information for chronic weight management medications¹⁰⁻¹² Phentermine/topiramate ER (Qsymia[®])

Dosing	Dose adjustments (if applicable)	Monitoring	Common side effects ¹¹	Contraindications ¹¹	Warnings
 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 If after 12 weeks the patient has not lost at least 5% of baseline body weight, discontinue by gradually tapering (taking a dose every other day for ≥1 week before stopping to avoid precipitating a seizure), as it is unlikely that the patient will achieve and sustain clinically meaningful weight loss with continued treatment 	 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 	 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 	 Increased heart rate Paresthesia Dizziness Dysgeusia Headache Insomnia Decreased serum bicarbonate Xerostomia Constipation Upper respiratory tract infection Naso- pharyngitis 	 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®)

Dosing Dose (if app	adjustments plicable)	Monitoring	Common side effects ¹¹	Contraindications ¹¹	Warnings
 Naltrexone 8 mg/bupropion 90 mg tablet dose escalation schedule: Morning Evening Week 1: 1 tablet None Week 2: 1 tablet 1 tablet Week 3: 2 tablets 1 tablet Week 24: 2 tablets 2 tablets Maintenance dose: Naltrexone 16 mg/bupropion 180 mg (2 tablets) twice a day Discontinue if 5% weight loss is not achieved by week 12 as it is unlikely that a meaningful weight loss will be achieved and sustained with continued treatment Dase i impair Mod rena maxi record dose morning to point tablet Not ti Mod rena maxi record dose Not ti Maxi Maxi 	in renal rment: derate or severe l impairment: imum mmended daily e is one tablet each ning and evening recommended use in patients end-stage l disease in hepatic rment: imum mmended daily e of naltrexone/ ropion is one et in the morning	 Weight Pregnancy tests in women of child-bearing potential as deemed necessary 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) Blood pressure and/or signs/symptoms of hyper- or hypotension Heart rate Signs and symptoms of depression, suicidal thought or behavior, cognitive impairment, or changes in mood 	 Headache Sleep disorder Nausea Constipation Diarrhea Vomiting Dizziness Xerostomia 	 Opioid use (agonists or partial agonists) Pregnancy Uncontrolled hypertension Seizure disorder Bulimia or anorexia nervosa Abrupt discontinuation of alcohol Acute opioid withdrawal Concomitant MAOI use or initiation in patients receiving linezolid or IV methylene blue 	 Suicidal thinking/ behavior [U.S. Boxed Warning] Neuropsychiatric symptoms May precipitate acute opioid with- drawal in patients receiving opioids Seizures Increase blood pressure, heart rate Hepatotoxicity Adjust hypoglycemia avoid hypoglycemia

Orlistat (Xenical[®], Alli[®])

Dosing	Dose adjustments (if applicable)	Monitoring	Common side effects ¹¹	Contraindications ¹¹	Warnings
 Xenical[®]: 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 Alli[®]: OTC labeling: 60 mg 3 times daily with each main meal containing fat 	• There are no dosage adjustments provided in the manufacturer's labeling	 Weight Blood pressure (orthostatic) and/or signs/symptoms of hypotension Glucose and/or signs/symptoms of hypoglycemia in patients with diabetes Liver function tests if signs or symptoms of hepatic dysfunction 	 Gastrointestinal effects (e.g., oily rectal leakage, abdominal distress/pain, flatulence with discharge, bowel urgency, steatorrhea) —typically frequency decreases over time Headache Fatigue Anxiety Menstrual disease Neuromuscular and skeletal pain 	 Pregnancy Chronic malabsorption syndrome Cholestasis 	 Increased urinary oxalate and nephrolithiasis Hepatotoxicity Cholelithiasis Interference with absorption of fat-soluble vitamins, cyclosporine, thyroid hormone, and anti-convulsants Adjust hypoglycemic medications to avoid hypoglycemia

Liraglutide (Saxenda®)

Dosing	Dose adjustments (if applicable)	Monitoring	Common side effects ¹¹	Contraindications ¹¹	Warnings
 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 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 	 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 Dose in renal impairment: Use with caution in renal impairment 	 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 endo- crine 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

Common drug interactions

Weight management medication	Interacting medication
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 Band (AGB)

Adjustable Gastric Banding^{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.



Vertical Sleeve Gastrectomy (VSG)



Biliopancreatic Diversion **(BPD)**

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 Switch¹⁴

- 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.



Biliopancreatic Diversion With a Duodenal Siwtch **(BPD-DS)**

• It retains the pylorus, minimizing problems related to dumping syndrome and marginal ulcer.

Important post-surgical considerations⁶



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

- 1. Leslie, W.S., C.R. Hankey, and M.E. Lean, Weight gain as an adverse effect of some commonly prescribed drugs: a systematic review. *Qjm*, 2007. 100(7): p. 395-404.
- 2. Bray, G.A. and D.H. Ryan, Medical therapy for the patient with obesity. *Circulation*, 2012. 125(13): p.1695-703.
- 3. Apovian C, A.L., Bessesen DH, et al., Pharmacological Management of Obesity: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*, 2015.100(2): p.342-362.
- 4. Perreault L, P.-S.F., Kunins L, Obesity in adults: etiology and risk factors. 2018, UpToDate: UpToDate.com.
- 5. Serretti, A. and L. Mandelli, Antidepressants and body weight: a comprehensive review and meta-analysis. *J Clin Psychiatry*, 2010. 71(10): p.1259-72.
- 6. Obesity, T.M.o.O.a. and W. Group, VA/DoD Clinical Practice Guideline for Screening and Management of Overweight and Obesity. 2014. Version 2.0.
- 7. Biener Al, D.S., Medical Care Use and Expenditures Associated With Adult Obesity in the United States. JAMA, 2018. 319(3): p.218.
- 8. Williams, E.P., et al., Overweight and Obesity: Prevalence, Consequences, and Causes of a Growing Public Health Problem. *Curr Obes Rep,* 2015.4(3): p.363-70.
- 9. Chapter 4: Active Adults, O.o.D.P.a.H. Promotion, Editor. 2008: health.gov.
- 10. Heymsfield, S.B. and T.A. Wadden, Mechanisms, Pathophysiology, and Management of Obesity. N Engl J Med, 2017. 376(3): p.254-266.
- 11. UpToDate. 2018, Lexicomp: UpToDate.com.
- 12. Pilitsi, E., et al., Pharmacotherapy of obesity: available medications and drugs under investigation. Metabolism, 2018.

- 13. Mechanick JI, e.a., Clinical Practice Guidelines for the Perioperative Nutritional, Metabolic, and Nonsurgical Support of the Bariatric Surgery Patient. *Obesity* (Silver Spring), 2014. 21(1): p.s1-27.
- 14. Neff KJ, O.T., le Roux CW, Bariatric surgery: the challenges with candidate selection, individualizing treatment and clinical outcomes. BMC Medicine, 2013. 11(8).
- 15. Vidal, J., et al., Long-term effects of Roux-en-Y gastric bypass surgery on plasma glucagon-like peptide-1 and islet function in morbidly obese subjects. *J Clin Endocrinol Metab*, 2009. 94(3): p.884-91.
- 16. Stano, S., et al., Effect of meal size and texture on gastric pouch emptying and glucagon-like peptide 1 after gastric bypass surgery. *Surg Obes Relat Dis*, 2017. 13(12): p.1975-1983.
- 17. Buzga, M., et al., Dietary intake and ghrelin and leptin changes after sleeve gastrectomy. *Wideochir Inne Tech Maloinwazyjne*, 2014. 9(4): p. 554-61.



U.S. Department of Veterans Affairs

Veterans Health Administration PBM Academic Detailing Service

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