Drugs available as adjuncts to diet and exercise for treatment of obesity

Generic name	Usual dosing (adults)	US DEA schedule	Adverse effects and precautions*
Pancreatic lipase inhibitor approved for long-term use			
Orlistat	120 mg 3 times daily with fat-containing meals. A reduced dose of 60 mg¶ is an option for patients who do not tolerate 120 mg.	Not a controlled substance	Cramps, flatulence, fecal incontinence, oily spotting, absorption of fat-soluble vitamins may be reduced. Rarely reported: severe liver injury, oxalate-kidney injury. Contraindicated during pregnancy.
Combination of phentermine-topiramate approved for long-term use			
Phentermine-topiramate	Initial: 3.75 mg phentermine/23 mg topiramate once daily in the morning for 14 days, followed by 7.5 mg phentermine/46 mg topiramate daily for 12 weeks. Then titrate based upon response: 11.25 mg phentermine/69 mg topiramate daily for 14 days, and then to a maximum dose of 15 mg phentermine/92 mg topiramate once daily.	C-IV (due to phentermine component)	Dry mouth, taste disturbance, constipation, paraesthesias, depression, anxiety, elevated heart rate, cognitive disturbances, insomnia (higher dose). Abuse potential due to phentermine component. Topiramate is teratogenic (increased risk of oral cleft defects, T1); negative pregnancy test prior to and during treatment and 2 forms of contraception necessary for women of child-bearing potential. Actions of topiramate component include inhibition of carbonic anhydrase; rarely metabolic acidosis and kidney stones may result from renal bicarbonate loss. Maximum dose with moderate hepatic or renal impairment (CrCl <50 mL/min) 7.5 mg phentermine/46 mg topiramate once daily. Upon discontinuation, tapering of dose over at least 1 week using every-other-day dosing is recommended.

			Contraindicated during pregnancy, hyperthyroidism, glaucoma, patients taking MAO inhibitors.
Combination of bupropion-naltrexone approved for long-term use			
Bupropion-naltrexone	Week 1: 1 tablet (8 mg naltrexone/90 mg bupropion) once daily. Week 2: 1 tablet twice daily. Week 3: 2 tablets in morning and one tablet in evening. Week 4: 2 tablets twice daily. Maximum daily dose: 4 tablets (32 mg naltrexone/360 mg bupropion).	Not a controlled substance	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth. Transient increase in blood pressure (1 to 2 mmHg on average) during initial 12 weeks of treatment; heart rate may also be increased. Contraindicated in patients with uncontrolled hypertension, seizure disorder, eating disorder, use of other bupropion-containing products, chronic opioid use, use within 14 days of MAO inhibitors, pregnancy, or breastfeeding.[Δ]
GLP-1 agonists approved for long-term use			
Liraglutide	Initial: 0.6 mg subcutaneously daily. Increase at weekly intervals (1.2, 1.8, 2.4, 3 mg) until recommended dose of 3 mg daily. If increased dose is not tolerated, consider delaying dose escalation by an additional week.[◇]	Not controlled substances	Nausea, vomiting, diarrhea, constipation, hypoglycemia in patients with T2DM (more common if used in conjunction with diabetes medications known to cause hypoglycemia), injection site reactions, increased lipase, increased heart rate. Rarely reported: pancreatitis, gallbladder disease, renal impairment, suicidal thoughts. Causes a modest delay of gastric emptying. Advise patients to avoid dehydration in relation to GI side effects. Monitor blood glucose in diabetic patients and adjust co-administered sulfonylureas (eg, reduce dose by 50%) and other anti-diabetic medications as needed to prevent potentially severe hypoglycemia. Possible increase in thyroid cancer risk based on murine model data. Contraindicated in pregnancy and in patients with a personal or family history of medullary thyroid cancer or multiple endocrine neoplasia 2A or 2B. For semaglutide, monitor patients with diabetic retinopathy for eye complications.
Semaglutide	Initial: 0.25 mg subcutaneously once weekly. Increase dose at 4-week intervals (0.5, 1, 1.7, 2.4 mg) until recommended dose of 2.4 mg weekly. If increased dose is not tolerated, consider delaying dose escalation by 4 weeks.[§]		

Noradrenergic sympathomimetic drugs approved for short-term use			
Benzphetamine	Initial: 25 mg once daily; may titrate up to 25 to 50 mg one to 3 times daily. Maximum dose: 50 mg 3 times daily.	C-III	Applies to all sympathomimetic agents: ▪ Due to their side effects and potential for abuse, we suggest **not** prescribing sympathomimetics for weight loss. ▪ If prescribed, limit to short-term (≤12 weeks) use. ▪ Adverse effects include increase in heart rate, blood pressure, insomnia, dry mouth, constipation, nervousness. ▪ Abuse potential due to amphetamine-like effects. ▪ May counteract effect of blood pressure medications. ▪ Avoid in patients with heart disease, poorly controlled hypertension, pulmonary hypertension, or history of addiction or drug abuse. ▪ Contraindicated in patients with a history of CVD, hyperthyroidism, glaucoma, MAO inhibitor-therapy, agitated states, pregnancy, or breast feeding.
Diethylpropion	Immediate release: 25 mg 3 times daily, 1 hour before meals. Controlled release: 75 mg every morning.	C-IV	
Phentermine	Immediate release: 15 to 37.5 mg daily or divided twice daily. Orally disintegrating tablet (ODT): 15 to 37.5 mg once daily in the morning. Immediate release (Lomaira): 8 mg 3 times daily before meals.	C-IV	
Phendimetrazine	Immediate release: 17.5 to 35 mg 2 or 3 times daily, 1 hour before meals. Maximum dose: 70 mg 3 times daily. Sustained release: 105 mg daily in the morning.	C-III	

Dosing in this table is for adults with normal kidney and liver function. Patients are reevaluated after 12 weeks on the maximum tolerated dose of a weight loss drug to determine efficacy.

CrCl: creatinine clearance; CVD: cardiovascular disease (arrhythmias, congestive heart failure, coronary artery disease, stroke, uncontrolled hypertension); GI: gastrointestinal; GLP-1: glucagon-like peptide 1; MAO inhibitors: monamine oxidase inhibitors; T1: first trimester pregnancy; T2DM: type 2 diabetes mellitus; US DEA: United States Drug Enforcement Agency; FDA: US Food and Drug Administration.

* Applies to all drugs except orlistat: May increase risk of hypoglycemia in type 2 diabetics. For additional information on potential interactions of anti-obesity drugs with other medications, use Lexi-Interact program included with UpToDate.

¶ Orlistat 60 mg is available without a prescription in the United States and some other countries.

Δ FDA recommends warning young adults (age 18 to 24 years) of the risk of becoming suicidal during initial treatment of psychiatric disorders with any antidepressant.

◇ According to United States labeling, if weight loss is not ≥4% after 16 weeks or 3 mg/day is not tolerated, discontinue use. Labeling in the European Union recommends discontinuation of use if weight loss is not ≥5% after 12 weeks of 3 mg/day.

§ According to United States labeling, if 2.4 mg/week is not tolerated, discontinue use.

Courtesy of authors.

With additional data from:

1. *The US National Library of Medicine DailyMed website. Availablet at: https://dailymed.nlm.nih.gov/dailymed/ (Accessed October 8, 2014).*
2. *Kim GW, Lin JE, Blomain ES, Waldman SA. Antiobesity pharmacotherapy: new drugs and emerging targets. Clin Pharmacol Ther 2014; 95:1.*
3. *US Food and Drug Administration. FDA approves new drug treatment for chronic weight management, first since 2014. 2021. Available at: https://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-treatment-chronic-weight-management-first-2014 (Accessed on June 8, 2021).*

Graphic 86204 Version 21.0