Obesity Pharmacotherapy: Quick Reference Guide

Anti-Obesity Medications Approved for Long-Term Use[1,2]

Who Are They For?

- Adults with a BMI ≥ 30
- Adults with a BMI ≥ 27 with ≥ 1 obesity-related comorbidity (eg, T2D, hypertension, dyslipidemia)
- *Orlistat: Also indicated for patients aged > 12 years with initial BMI ≥ 30 or ≥ 27 with other risk factors*
- *Liraglutide: Also indicated for pediatric patients aged > 12 years with body weight > 60 kg **and** initial BMI corresponding to 30 for adults*

Summary of Available Agents[a]

	Orlistat (Xenical®)	Naltrexone/ Bupropion (Contrave®)	Phentermine/ Topiramate (Qsymia®)	Liraglutide 3.0 mg (Saxenda®)	Semaglutide 2.4 mg (Wegovy®)
Maximum dose	120 mg orally, 3× daily	32/360 mg orally, daily	15/92 mg orally, daily	3 mg SC, daily	2.4 mg SC, weekly
Common adverse events (≥ 5%)	Oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, increased defecation, fecal incontinence	Nausea, constipation, headache, vomiting, insomnia, dry mouth, dizziness, diarrhea	Paresthesia, dizziness, dysgeusia, insomnia, constipation, dry mouth	Nausea, diarrhea, constipation, vomiting, injection site reactions, headache, dyspepsia, hypoglycemia, fatigue, dizziness, abdominal pain, increased lipase, upper abdominal pain, pyrexia, gastroenteritis	Nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distension, eructation, hypoglycemia in patients with T2D, flatulence, gastroenteritis, gastroesophageal reflux disease
Drug interactions	Alcohol, cyclosporine, digoxin, fat-soluble vitamin supplements and analogues, glyburide, levothyroxine	Agents metabolized by CYP2D6 enzyme, CYP2B6 inhibitors or inducers, dopaminergic drugs, digoxin, MAOIs, agents that lower seizure threshold	Oral contraceptives, CNS depressants including alcohol, non-potassium sparing diuretics	May affect absorption of medications due to slowing of gastric emptying	May affect absorption of medications due to slowing of gastric emptying
Key Contra-indications	Chronic malabsorption syndrome, cholestasis	Uncontrolled hypertension, opioid use, history or risk for seizure, abrupt discontinuation of alcohol, concomitant MAOI Not recommended in severe hepatic impairment, ESRD	Glaucoma, hyperthyroidism, during or within 14 days of taking MAOIs	Personal or family history of MTC or MEN-2	Personal or family history of MTC or MEN-2

Use not recommended in pregnant or breastfeeding women, or in those trying to conceive

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How Should Anti-Obesity Medications be Used?

Start with initial dose then **escalate** as indicated

Monitor for efficacy, safety and tolerability during titration. Safety or tolerability issues arise → discontinue[b]

At 12 to 16 weeks:
≥4% to 5% weight loss achieved → continue.
≥4% to 5% weight loss ***not*** achieved → discontinue, consider alternative anti-obesity medication or treatment.

Medications for other comorbidities (eg, antidepressants, steroids, glucose-lowering therapies) may be contributing to weight gain; consider changing to a weight-neutral or weight-reducing alternative if suitable

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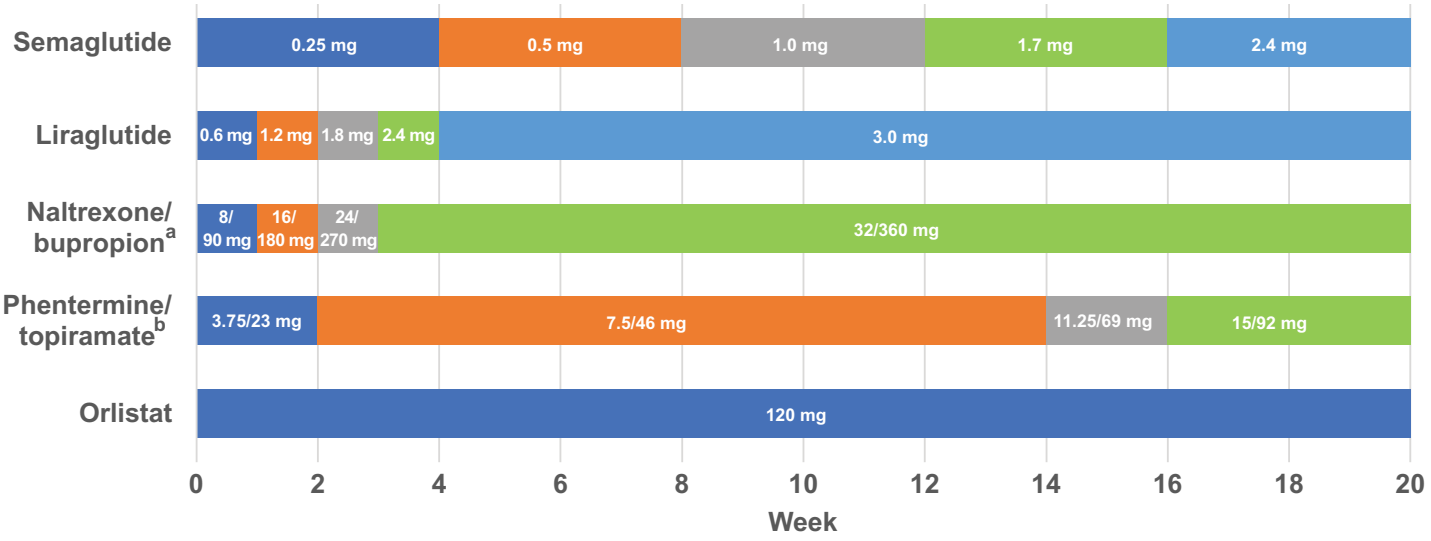
[a]Setmelanotide is also available for chronic weight management in adult and pediatric patients aged ≥ 6 years with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency confirmed by genetic testing;[1] [b]Phentermine/topiramate must be discontinued gradually to prevent possible seizure.[1] BMI, body mass index; CNS, central nervous system; ESRD, end-stage renal disease; MAOI, monoamine oxidase inhibitor; MEN-2, multiple endocrine neoplasia syndrome type 2; MTC, medullary thyroid carcinoma; SC, subcutaneous; T2D, type 2 diabetes.

1. Drugs@FDA. Accessed February 18, 2022. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm; 2. Obesity Canada. Canadian Adult Obesity Clinical Practice Guidelines. Accessed February 18, 2022. https://obesitycanada.ca/guidelines/chapters

Initiation and Titration of Anti-Obesity Medications

Most obesity medications have specific titration profiles that are indicated to minimize AEs and that can last from a few weeks to several months.[1] Titration may take longer in pediatric versus adult patients and maximum tolerated doses also differ.[1] Medications should be initiated at a lower dose and not uptitrated to the maintenance dose until they are well tolerated.[1] If someone does not take their medication for a period of several days, it may be necessary to reinitiate treatment at a lower dose and titrate up to the maximum tolerated dose again.[1]

Anti-Obesity Medication Titration Schedules[1]



Dose Escalation and Missed Dose Management[1]

	Semaglutide 2.4 mg	Liraglutide 3.0 mg	Phentermine/ Topiramate	Naltrexone/ Bupropion	Orlistat
During dose escalation	• If dose not tolerated, consider delaying dose escalation for 4 weeks • If maintenance 2.4 mg once-weekly dose not tolerated, temporarily decrease to 1.7 mg once weekly, for max. of 4 weeks. After 4 weeks, increase to maintenance 2.4 mg once weekly	**Adult:** • If dose not tolerated, consider delaying dose escalation for 1 week **Pediatric:** • If dose not tolerated, dose can be lowered to previous level; dose escalation may take up to 8 weeks • If 3.0 mg daily dose not tolerated, maintenance dose can be reduced to 2.4 mg daily	If patient has not lost ≥ 3% of baseline body weight on 7.5 mg/ 46 mg dose, discontinue or escalate dose.	N/A	N/A
Missed doses	**1 dose:** if next scheduled dose is > 2 days away (48 hours), administer a dose as soon as possible. If next scheduled dose < 2 days away (48 hours), do not administer a dose. Resume dosing on regularly scheduled day of week. **> 2 consecutive doses:** resume dosing as scheduled or, if needed, reinitiate and follow the dose escalation schedule (reduce occurrence of GI symptoms).	**1 dose:** resume once-daily regimen with next scheduled dose. Do not administer extra dose or increase dose to make up for missed dose. **> 3 doses:** reinitiate at 0.6 mg daily and follow recommended dose escalation schedule to reduce occurrence of GI adverse reactions.	**1 dose:** wait until the next morning to take usual dose. Do not double the dose.	**1 dose:** wait until next scheduled dose to resume regular dosing schedule.	N/A

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[a]Extended-release tablets: 8 mg naltrexone / 90 mg bupropion; 1 tablet = dosed in the morning, 2 tablets = 1 tablet in morning + 1 in evening, 3 tablets = 2 tablets in morning + 1 in evening, 4 tablets = 2 tablets in morning + 2 in evening; [b]Dosed in the morning with or without food. Avoid dosing with phentermine/topiramate in the evening due to the possibility of insomnia. The 3.75 mg/23 mg and 11.25 mg/69 mg doses are for titration purposes only. AE, adverse event; GI, gastrointestinal.

1. Drugs@FDA. Accessed February 18, 2022. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm.

Managing Adverse Events with Anti-Obesity Medications

Certain signs and symptoms that patients may experience when using an anti-obesity medication indicate a need to contact an HCP and, in some cases, discontinue medication immediately.[1] Inform patients of what they need to look for and what to do if any occur. Details of agent-specific serious adverse events and the related signs and symptoms can be found in the patient information leaflet that comes with the medication.

General Signs and Symptoms Indicating a Need to Contact an HCP Immediately[1]

Serious allergic reactions
Swelling of face, lips, tongue or throat, severe rash or itching, very rapid heartbeat, problems breathing or swallowing, fainting or feeling dizzy

Changes in vision
Sudden decrease in vision with or without eye pain and redness, a blockage of fluid in the eye causing increased pressure, swelling or redness around the eye

Kidney problems (kidney failure)
Persistent nausea, vomiting, or diarrhea, or inability to drink liquids by mouth

Pancreatitis
Severe pain in stomach area (abdomen) that will not go away, with or without vomiting; may feel pain from abdomen to back

Increased risk of hypoglycemia
Especially if already taking medications for diabetes

Depression, suicidal actions or thoughts
Sudden changes in mood, behaviors, thoughts, or feelings that are new, worse, or worrisome

Increased heart rate
Heart racing or pounding in chest that lasts for several minutes

Severe liver problems
Jaundice, dark/amber-colored urine, pain in upper right quadrant of abdomen

Gallbladder problems
Pain in upper abdomen, jaundice, fever, clay-colored stools, nausea, vomiting

Any adverse effect that is bothersome or does not resolve

Top Tips for Managing GI Adverse Events with Liraglutide 3.0 mg and Semaglutide 2.4 mg

Simple steps to reduce the risk of GI adverse effects and support people in managing them:[2-4]

- **Titrate the dose slowly when possible**
- **Educate people to decrease their food intake and stop eating when full**
- **Advise people around limiting certain foods (eg, spicy meals or those with high fat content)**
- **Reassure people that events are transient and should decrease over time**

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1. Drugs@FDA. Accessed February 18, 2022. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm; 2. Hinnen D. *Diabetes Spectr*. 2017;30:202-210; 3. Nauck MA, et al. *Mol Metab.* 2021;46:101102; 4. Romera I, et al. *Diabetes Ther.* 2019;10:5-19.
GI, gastrointestinal.

Top Tips for Effective Communication and Education[1-4]

Effective communication and education can help ensure optimal safety and outcomes for patients.[1-5]

Offer multiple touch points for communication

- ✓ Assess patient and caregiver learning styles – ask about preferences
- ✓ Offer educational materials in different formats (eg, video, printed handbook, website)
- ✓ Use a mixture of online and offline formats (eg, answering questions over the phone, using secure email or messaging)

Consider social and cultural backgrounds

- ✓ Social and cultural backgrounds may influence perspectives, values, beliefs, and health behaviors
- ✓ Build trust and respect by asking individuals and their caregivers about their cultural beliefs
- ✓ Remain open and non-judgmental

Use the "Teach Back" method

- ✓ Ask patients/carers to reiterate information provided
- ✓ Avoid saying "Did you understand?" or "Does that make sense?"
- ✓ Instead, try, "Show me how you would..." or "What would you do if _____happened?"
- ✓ Listen actively; confirm and acknowledge correct answers and clarify any points as needed

Encourage questions

- ✓ Ask open-ended questions (eg, "What questions do you have?" or "What would you like me to clarify?")
- ✓ Avoid closed, yes/no prompts that do not facilitate dialogue (eg, "Do you have any questions?")
- ✓ Direct people to helpful resources, like the AHRQ's "10 Questions You Should Know"

Assess health literacy

- ✓ Health literacy is the degree to which a person can obtain, communicate, process, and understand health information in order to make informed care decisions
- ✓ Ensure patients can read their prescription labels/materials, follow treatment instructions, complete applications or forms
- ✓ Health literacy is independent of literacy in other fields, but can be influenced by age, location, education

Keep discussions short and simple

- ✓ Break detailed information into digestible chunks
- ✓ Use plain/lay language instead of medical jargon
- ✓ Give specific instructions (eg, "Take 1 tablet 2 hours before eating your dinner," rather than, "Take your medication on an empty stomach")
- ✓ Use visual aids (eg, a handout with a diagram, a demonstration of a technique or device)

3 Focus on 3 key points

- ✓ Limit your discussions to 3 main points; offer written handouts or instructions with further information
- ✓ Ask people about their questions and concerns
- ✓ Summarize the key points at the end of the discussion to reinforce the key points made

Provide easy-to-read materials

- ✓ Define and explain complex information
- ✓ Use simple instructions or disease-specific care plans
- ✓ Use plain language with simple well-known terms
- ✓ Use large, easy-to-read fonts and lots of white space
- ✓ Include diagrams or simple illustrations
- ✓ Include pharmacy contact information

1. Agency for Healthcare Research and Quality. The impact of communication on medication errors. Accessed February 18, 2022; https://psnet.ahrq.gov/web-mm/impact-communication-medication-errors; 2. Sassoli M, Day G. *Asia Pac J Health Manage*. 2017;12:47-61; 3. Digital Pharmacist. Accessed February 18, 2022. https://www.digitalpharmacist.com/blog/patient-communication-for-pharmacy/; 4. Agency for Healthcare Research and Quality. Approach to improving patient safety: Communication. Accessed February 18, 2022. https://psnet.ahrq.gov/perspective/approach-improving-patient-safety-communication; 5. Elliot M, Liu Y. *Br J Nurs*. 2010;19(5):300-305.