Why Wait?
A Provider's Guide to Weight Management Pharmacotherapy

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Objectives

1. Compare the pharmacotherapy options for weight management
2. Examine clinical factors to consider when initiating and titrating weight management therapy
3. Discuss the current barriers to use of weight management pharmacotherapy

Obesity Overview

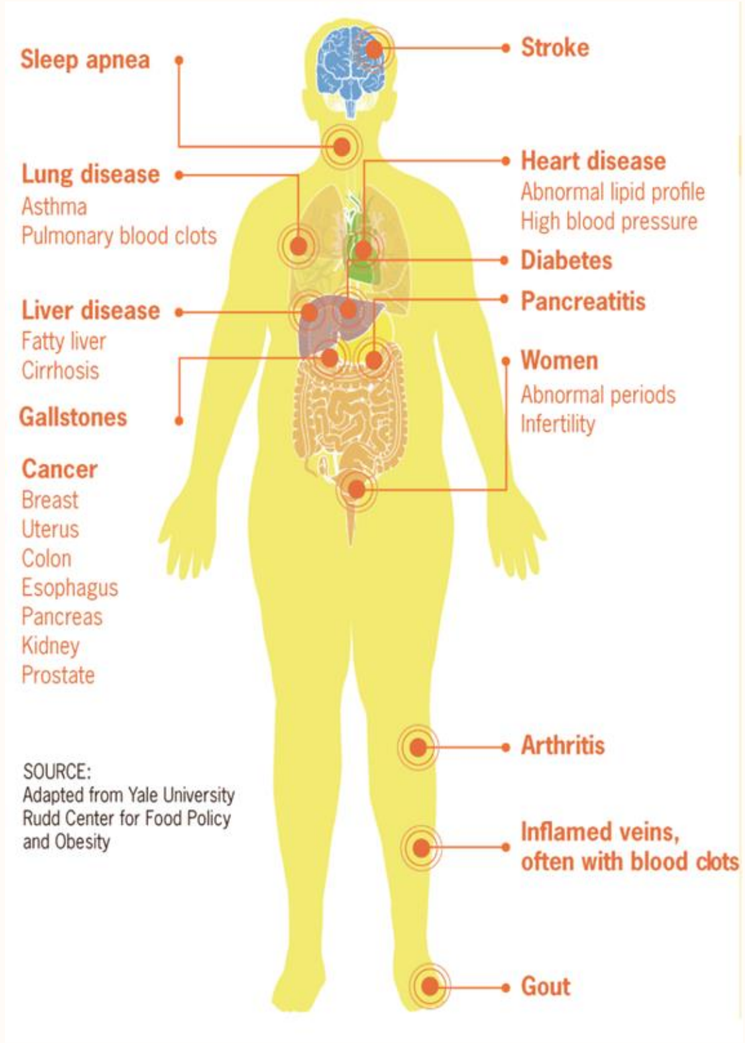
- Recognized as a chronic disease by the American Medical Association (AMA) in 2013
- Causes: eating patterns, physical activity levels, sleep routines, genetics, social determinants of health, medications
- Prevalence:
  - Adults: 30.5% in 1999-2000 → 41.9% in 2017-2020
  - Young adults: 6.2% in 1976-1980 → 33% in 2017-2018
- Cost to the U.S. healthcare system: ~$173 billion/year (in 2019 dollars)

Obesity Screening + Diagnosis

- 2025 AACE Consensus Statement
  - Recommends Adiposity-Based Chronic Disease (ABCD) as a diagnostic term for obesity
  - Outlines classifications by stages and presence of Obesity-Related Complications and Diseases (ORCD)

ABCD Stage	Description
1 (pre-clinical obesity)	No known obesity-related cardiometabolic, biomechanical, or other psychological disease
2	≥ 1 mild/moderate ORCD
3	At least one severe ORCD

Obesity-Related Complications



Obesity Classifications

Classification	BMI (kg/m^2)
Overweight	25-29.9
Class I Obesity	30-34.9
Class II Obesity	35-39.9
Class III Obesity	≥ 40

Pharmacotherapy Options

Patient Eligibility for Pharmacotherapy

- *Historical Requirement* - Inadequate response to lifestyle interventions
- BMI ≥30 kg/m^2
- BMI ≥27 kg/m^2 with ≥1 weight-related complication
  - Diabetes, prediabetes, hypertension, dyslipidemia, etc.
- Assessment of readiness to change
- Not currently pregnant (contraindication for all medications)

Discuss referral for bariatric surgery in patients with BMI ≥ 35 mg/m^2 or BMI ≥ 30 mg/m^2 with cardiometabolic disease with or without previous use of pharmacotherapy

Goals of Pharmacotherapy

- Achieve sufficient weight loss needed for clinical improvement

≤ 5% (at 3-6 months)	→	> 5% to 15%	→	> 15%

• Incomplete response
• Consider discontinuation
		• Good response
		• May see improvement in certain ORCDs once more than 10% lost
		  • T2DM, OSA, MACE, ASCVD, osteoarthritis
				• Excellent response
				• May treat or prevent broad range of ORCDs
				  • HTN, dyslipidemia, MASH, PCOS

FDA Approved Agents

1. Tirzepatide
2. Semaglutide
3. Liraglutide
4. Phentermine
5. Phentermine-Topiramate
6. Naltrexone-Bupropion
7. Orlistat

Second-generation medications

First-generation medications

Pharmacotherapy Categories

Neuromodulators	Digestion Modulators	Hormone Modulators
• Phentermine-topiramate • Naltrexone-bupropion • GLP-1 and GLP-1/GIP receptor agonists	• GLP-1 and GLP-1/GIP receptor agonists • Orlistat	• GLP-1 and GLP-1/GIP receptor agonists
↓	↓	↓
Decrease appetite, cravings, and impulse/reward seeking behaviors	Decrease nutrient absorption or slow digestion	Enhance insulin sensitivity, increase GLP-1/GIP effect

General Pharmacotherapy Considerations

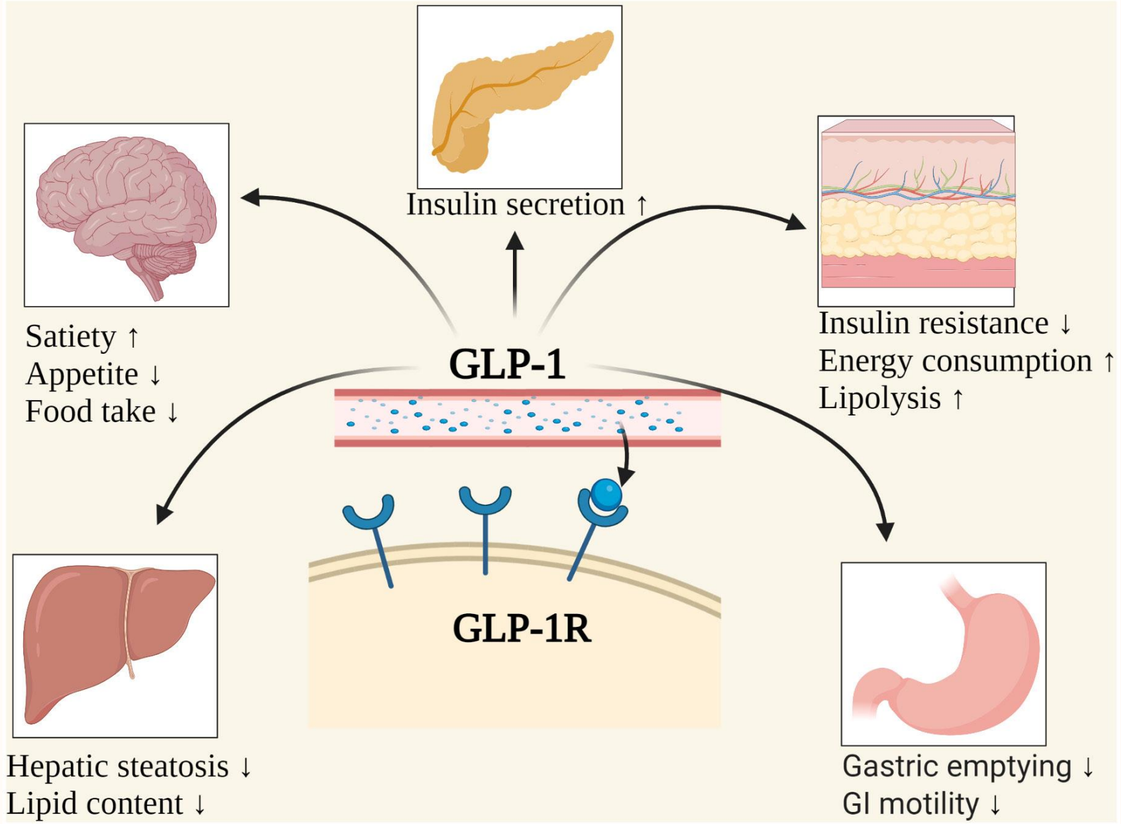
- Discontinue the agent if ≥ 5% TBWL is not seen after 3 months of the highest tolerated dose
- Complete tolerability and efficacy check-ins during titration phase

Choose an agent based on:

- Contraindications
- Insurance Coverage/Cost
- Comorbidities
- Symptom Targets
- Goals of Therapy

Hormone Receptor Agonists

- Semaglutide (Wegovy®)
  - GLP-1 Receptor Agonist
- Liraglutide (Saxenda®)
  - GLP-1 Receptor Agonist
- Tirzepatide (Zepbound®)
  - GLP-1/GIP Receptor Agonist
    - GIP agonism has synergistic effects with GLP-1 agonism



https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2023.1085799/full

Hormone Receptor Agonists

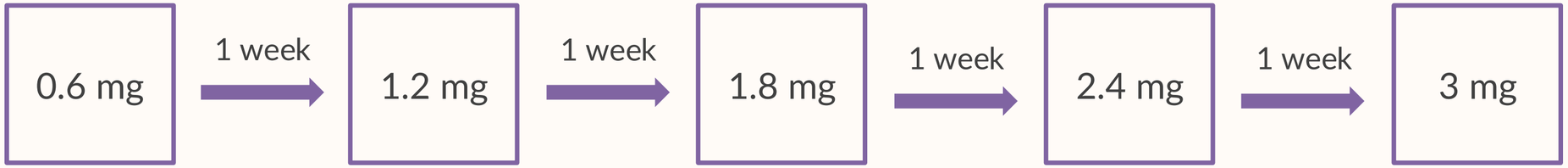
- Contraindications
  - Personal or family history of medullary thyroid cancer or MEN2
- Caution
  - History of gastroparesis
  - History of pancreatitis
    - Consider cause of pancreatitis and if risk factor(s) have been eliminated

Hormone Receptor Agonists

- Adverse Effects
  - Nausea, vomiting, diarrhea
    - Mitigate by eating smaller, more frequent meals and avoiding high fat, overly sweet foods
  - Muscle and bone loss
    - Secondary to rapid weight reduction
  - Constipation
    - Mitigate by increasing fiber and water intake
  - Hypoglycemia
    - Low risk as insulin secretion is stimulated through a glucose-dependent manner

Liraglutide (Saxenda®)

- Once daily subcutaneous injection



Multi-Use Self-Injectable Pen

Must prescribe pen needles!

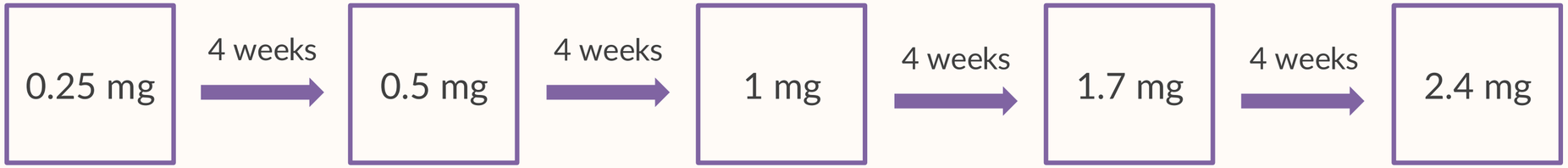
novomedlink.com/obesity/products/treatments/wegovy/dosing-administration/the-wegovy-pen.html

Liraglutide (Saxenda®)

- Dosing considerations
  - Patients receive box of 3 pens (9 mL) or 5 pens (15 mL) that dial to any of the doses in the titration schedule
  - If patients are having intolerable side effects, consider extending the titration schedule (as insurance allows)
  - The recommended maintenance dose is 3 mg

Semaglutide (Wegovy®)

- Once weekly subcutaneous injection



Single-dose autoinjector

novomedlink.com/obesity/products/treatments/wegovy/dosing-administration/the-wegovy-pen.html

Semaglutide (Wegovy®)

- Dosing considerations
  - Patients receive box of 4 pens (28-day supply)
  - If patients are having intolerable side effects, consider extending the titration schedule (as insurance allows)
  - The recommended maintenance dose is 2.4 mg, but 1.7 mg can also be considered a maintenance dose

Semaglutide (Wegovy®)

- Once daily **oral tablet** (approved 12/22/2025)

- Administration is very important for efficacy
  - Take with a sip of water (up to 4 ounces) on an empty stomach and wait at least 30 minutes before eating, drinking, or taking other medications

Semaglutide (Wegovy®)

- Additional indications
  - *Injectable only* - Noncirrhotic metabolic dysfunction–associated steatohepatitis in adults with moderate to advanced liver fibrosis (stages F2 to F3)
    - No specific BMI criteria in the clinical trial, but data for BMI < 25 kg/m^2 is limited
  - *Injectable and oral* - Risk reduction of major adverse cardiovascular events in adults with established cardiovascular disease and either obesity or overweight

Tirzepatide (Zepbound®)

- Once weekly subcutaneous injection

Single-dose autoinjector

https://zepbound.lilly.com/how-to-use

Tirzepatide (Zepbound®)

- Dosing considerations
  - Dual GLP-1/GIP better tolerated?
  - Patients receive box of 4 pens (28-day supply)
  - If patients are having intolerable side effects, consider extending the titration schedule (as insurance allows)
  - The recommended maintenance doses are 5 mg, 10 mg, 15 mg
    - Consider maintaining on the lowest maintenance dose if achieving sufficient weight loss
- Additional indication
  - Treatment of moderate to severe obstructive sleep apnea (AHI≥ 15) in adults with obesity
    - Maintenance dose of 10 or 15 mg

Hormone Agonists – Clinical Pearls

- Counsel patients appropriately on purpose of these agents
  - To be used alongside changes in lifestyle
- Considered long-term therapy and not a quick fix
- Ensure adequate nutrition to prevent metabolic slowing and nutritional deficiencies
  - Low threshold to refer to a dietician
- Ensure adequate resistance training and protein intake to prevent excess muscle and bone loss

Hormone Agonists – Clinical Pearls

- Stay on top of hydration
  - GLP-1 hormone can reduce thirst drive
- Ask about pregnancy plans or use of contraception
  - Consider effects on hormonal contraception
  - Recommended to stop therapy 2 months prior to trying to conceive

Phentermine

- Sympathomimetic; reduces appetite and increases metabolism
- Schedule IV controlled substance
- Contraindications
    - History of cardiovascular disease
    - Hyperthyroidism
    - Glaucoma
    - Agitated states
    - History of drug abuse
    - Use of monoamine oxidase inhibitors (MAOIs) within 14 days
    - Breastfeeding

Phentermine

- Adverse effects
  - Cardiovascular – increased blood pressure and heart rate
  - CNS – anxiety, insomnia, irritability, delirium, psychosis
- Dosing
  - Dosing can vary, but typically 37.5 mg in 1 or 2 divided doses
    - Take on an empty stomach (30 minutes before or 1 hour after eating) for best absorption
  - Lomaira® → 8 mg three times daily 30 minutes before meals

Phentermine

- Ohio Law Updates
  - Can now prescribe long-term given that:
    - At least 5% TBWL achieved within 3 months after initiation and assessed by prescriber every 3 months while on therapy
- Clinical Pearls
  - Long-term safety and effectiveness?
  - Can be efficacious for patients who have “hungry brain”
  - Ensure breakfast is not skipped as appetite will be suppressed

Phentermine-Topiramate (Qsymia®)

- Addition of topiramate – decrease in cravings, appetite suppression, and enhancement of satiety
- Schedule IV controlled substance with REMS program
  - Known teratogenic
- Contraindications
  - Hyperthyroidism
  - Glaucoma
  - Use of MAOIs within 14 days
- Caution
  - History of kidney stones

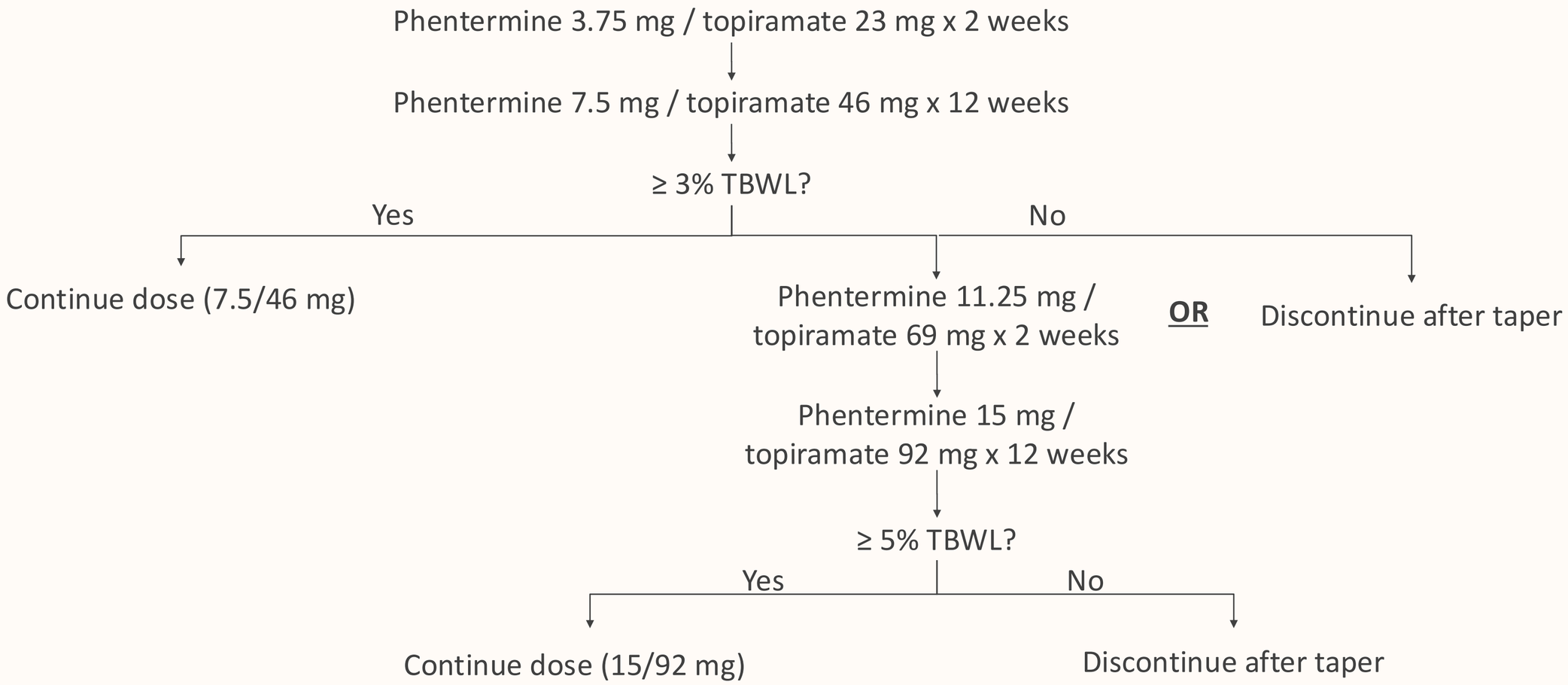
Phentermine-Topiramate (Qsymia®)

- Adverse effects
  - Insomnia
  - Increased blood pressure
    - Clinical trials showed blood pressure decline
  - Increased heart rate, palpitations
    - Clinically insignificant increase in clinical trials
  - Cognitive impairment, constipation, dry mouth

Phentermine-Topiramate (Qsymia®)

- Dosing
  - Once daily in the morning
  - Complex titration schedule
    - Evaluate safety and efficacy at each dose
  - Taper upon discontinuation to limit risk of seizures
    - 1 capsule every other day for 1 week then stop
- Clinical pearls
  - Lower doses of phentermine – less cardiovascular effects?
  - Savings options for cash paying patients
    - Both brand-name and generic options available

Phentermine-Topiramate (Qsymia®)



Bupropion-Naltrexone (Contrave®)

- Regulate food intake and mesolimbic reward pathways
- Contraindications
  - Chronic opioid therapy or need for short-term opioids
  - Uncontrolled hypertension
  - History or risk of seizures
  - Bulimia or anorexia nervosa
  - Abrupt discontinuation of drugs or alcohol
  - Use of MAOIs within 14 days, linezolid, or IV methylene blue
- Adverse effects
  - Nausea, vomiting, constipation, headache, dizziness, increased blood pressure

Bupropion-Naltrexone (Contrave®)

- Oral tablets containing 8 mg naltrexone / 90 mg bupropion

- Clinical pearls
  - Savings options for cash paying patients
  - Side effects, particularly to the naltrexone component, can limit use
  - Review drug interactions

Orlistat

- Inhibits gastric and pancreatic lipases to decrease dietary fat absorption
- Contraindications
  - Chronic malabsorption syndrome
  - Cholestasis
- Adverse effects
  - Abdominal pain, flatulence, oily stools, fecal urgency/incontinence
  - Vitamin deficiencies - administer multivitamin daily (2 hours apart from orlistat)
- Dosing
  - Take with fat-containing meals
    - Alli® (OTC) → 60 mg three times daily
    - Xenical® (Rx) → 120 mg three times daily

Orlistat

2022 American Gastroenterological Association Guidelines recommend *against* use given limited weight loss benefit with significant gastrointestinal side effects

Off-Label Options

- Consideration could be made for prescribing of bupropion, topiramate, and/or naltrexone as individual medications
  - Can mimic dosing of the combination agents or customize dosing based on symptom control and to limit side effects
- Cost saving option for patients without coverage for weight loss agents
- Single agent considerations:
  - Naltrexone is only available in 50 mg tablets so difficult to mimic Contrave® dosing; no weight loss data as monotherapy (without bupropion)
  - Topiramate can cause fatigue; dose in the evening
  - If using bupropion XL, dose in the morning

Therapy Selection

General Pharmacotherapy Considerations

Choose an agent based on:

- Contraindications
- Insurance Coverage/Cost
- Comorbidities
- Symptom Targets
- Goals of Therapy

Insurance Coverage/Cost

- Ohio Medicaid
  - Not covered when used for *obesity* alone
  - Coverage for Wegovy® in patients ≥ 45 years old with history of myocardial infarction, stroke, or peripheral artery disease
  - Coverage for Zepbound® in obese patients with moderate-to-severe obstructive sleep apnea
- Medicare
  - Not covered when used for *obesity* alone
  - Some plans cover Wegovy® for obese/overweight patients with established cardiovascular disease or Zepbound® for obese patients with moderate-to-severe obstructive sleep apnea
  - Wegovy® is on the list of negotiated drugs for 2027

Insurance Coverage/Cost

- Commercial insurance coverage varies
  - Coverage has become increasingly limited for hormone receptor agonists given cost to health plan
  - Typical prior authorization criteria:
    - ≥ 30 or ≥ 27 with weight-related comorbidities
    - 3 to 6-month trial of lifestyle modifications
    - No concurrent FDA-approved weight loss agents
    - Continued lifestyle modifications with use of agent

Cost Without Insurance Coverage

- Off-label generic agents (bupropion, naltrexone, phentermine, and topiramate) are relatively inexpensive
  - ~$10-30/month without insurance
- Contrave® and Qsymia® are available through their respective manufacturers for ~$100/month
  - Phentermine/topiramate is available at local pharmacies for ~$40-80/month

Cost Without Insurance Coverage

Agent	Type	Cost per Month	Source	Notes
Tirzepatide	Vial	$299 (2.5 mg) $399 (5 mg) $449 (7.5, 10, 12.5, 15 mg)	LillyDirect	• 7.5 mg and above must be filled every 45 days for reduced cost
Tirzepatide	Pen	~$499 (all strengths)	LillyDirect or Local Pharmacy	• If filling at local pharmacy, must use copay card and cannot have government sponsored plan
Semaglutide	Pen	$349 (all strengths)	NovoCare or Local Pharmacy	• New patients eligible for $199/month for first 2 months • At local pharmacy, cannot have government sponsored plan
Semaglutide	Tablet	$149 (1.5, 4 mg) $299 (9, 25 mg)	NovoCare or Local Pharmacy	• At local pharmacy, cannot have government sponsored plan
Liraglutide	Pen	$200-700 on GoodRx® (depending on prescribed dose)	Local Pharmacy	• Cost will vary depending on pharmacy • Supply may be limited as generic is only produced by one manufacturer

Comorbidities & Symptom Targets

Agent	Comorbidities/Patient Characteristics	Symptom Targets
Hormone Agonists	Insulin resistance (T2DM, pre-DM, PCOS, perimenopause), HF, ASCVD, CKD, OSA, MASH	Appetite suppression
Bupropion	Depression, low energy, nicotine use, emotional eating, inattention	Appetite suppression, increase metabolic rate
Naltrexone	Alcohol misuse	
Phentermine	Inattention	Appetite suppression, increase metabolic rate
Topiramate	Migraines, insomnia, binge-eating	Decrease soda/sugar intake

Goals of Therapy

Agent	Trial	Patient Population	Dose	Time Frame	%TBWL
Tirzepatide	SURMOUNT-1	Overweight or obese + lifestyle changes	15 mg	72 weeks	22.5%
Semaglutide (injectable)	STEP 1		2.4 mg	68 weeks	16.9%
Semaglutide (oral)	OASIS-4		25 mg	64 weeks	13.6%
Phentermine-topiramate	CONQUER		15/92 mg	56 weeks	9.8%
Liraglutide	SCALE		3 mg	56 weeks	8.0%
Naltrexone-bupropion	COR-I		32/360 mg	56 weeks	6.1%
Phentermine	Meta-analyses	Varied	Varied	Varied	5.5-7.7%
Orlistat	XENDOS	Obese + lifestyle changes	360 mg	4 years	5.8 kg

*TBWL = total body weight loss

Hormone Agonist Compounding

- FDA resolved shortages of semaglutide and tirzepatide in spring 2025
  - Compounded agents are in violation of the FDA unless they have made changes to the medication (additives, dose, etc.)
  - The compounded agents are not FDA approved for safety, efficacy, or quality
- Concerns with the compounded versions include improper storage, fraudulent drugs, dosing errors, adverse effects

Ongoing Monitoring

Follow-Up Visits

- Discuss symptom control
  - Appetite suppression, hunger, cravings
- Celebrate scale and non-scale victories
- Review any side effects and ways to mitigate
- Set goals for exercise and nutrition
  - Consider referral to dietician for specific caloric intake or macronutrient goals
  - Review step counts or minutes spent strength training or participating in aerobic exercise

Follow-Up Visits

- Optimize management of comorbid conditions that can make weight loss more difficult
  - Mood disorders, diabetes, OSA, etc.
- Reduce or eliminate weight positive medications as able
  - Insulin, steroids, contraceptives, etc
- Monitor co-morbid conditions for potential changes in pharmacotherapy/management with weight loss
  - Reduction in BP meds? Or DM meds?
  - Check TSH in patients with hypothyroidism on treatment

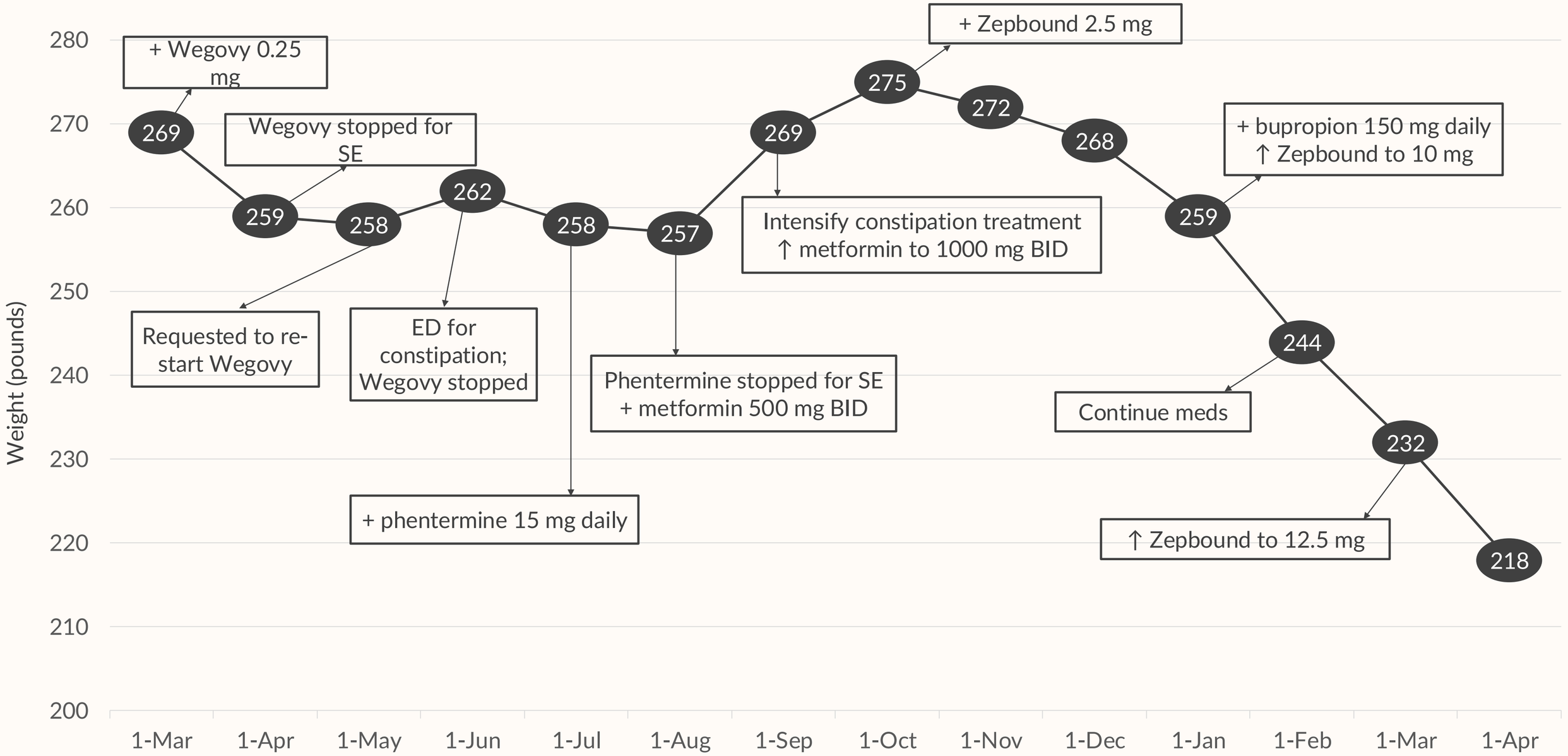
Duration of Therapy

- Ensure the patient is responding appropriately to therapy
  - If they have not achieved > 5% TBWL after 3 months of the highest tolerated dose, discontinue or augment the agent
- Most clinical trials had patients on the agents for more than 1 year
  - Use of these agents is not a quick-fix and must consider the long-term nature of the medications
  - Obesity is a chronic disease and suggests need for ongoing treatment to maintain weight loss
- Weight regain can be seen after discontinuation of the agents
  - Ensure exercise and nutrition are not forgotten!

Patient Case

Patient LA – 60-year-old female

- PMH: OSA on CPAP, prediabetes, endometrial cancer s/p hysterectomy, lumbar radiculopathy
- Initial weight: 269 lb, BMI 38.6 kg/m^2
- She read about “weight loss medications” and sister is on Ozempic; wanted to start on medications


Weight (pounds)
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1-Sep
1-Oct
1-Nov
1-Dec
1-Jan
1-Feb
1-Mar
1-Apr
269
+ Wegovy 0.25 mg
259
Wegovy stopped for SE
258
262
Requested to re-start Wegovy
ED for constipation; Wegovy stopped
258
+ phentermine 15 mg daily
257
Phentermine stopped for SE + metformin 500 mg BID
269
Intensify constipation treatment ↑ metformin to 1000 mg BID
275
+ Zepbound 2.5 mg
272
268
259
+ bupropion 150 mg daily ↑ Zepbound to 10 mg
244
Continue meds
232
↑ Zepbound to 12.5 mg
218

Review

Question 1

A 45-year-old female (on oral contraception) with a BMI of 33 kg/m² and a history of OSA, depression, kidney stones, and uncontrolled hypertension is seeking pharmacotherapy for weight management. She has tried lifestyle modifications but has not achieved significant weight loss.

Which of the following medications is the most appropriate for this patient?

A. Orlistat
B. Phentermine
C. Phentermine-topiramate (Qsymia®)
D. Bupropion-naltrexone (Contrave®)
E. Tirzepatide (Zepbound®)

Question 1

A 45-year-old female (on oral contraception) with a BMI of 33 kg/m² and a history of OSA, depression, kidney stones, and uncontrolled hypertension is seeking pharmacotherapy for weight management. She has tried lifestyle modifications but has not achieved significant weight loss.

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Question 2

You start Zepbound® for the patient in Question #1 and are seeing the patient in clinic four months later. Her current dose of Zepbound® is 10 mg weekly and she has lost ~16.7% of her baseline body weight (32 pounds). She is experiencing nausea for ~2 days after her injection and a decrease in hunger/cravings.

What is the most appropriate next step?

A. Decrease the dose to 7.5 mg weekly
B. Continue 10 mg weekly
C. Increase the dose to 12.5 mg weekly
D. Increase the dose to 15 mg weekly

Question 2

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Why Wait?
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