Best Practices in Obesity Management: The Role of New and Emerging Therapies

This program is supported by an educational grant provided by Novo Nordisk Inc.

Faculty

Disclosures

- Angela Golden
  Novo Nordisk: Speaker and Advisory Bureau
  Health-Script (Orexigen): Speaker’s Bureau

Learning Objectives

- Identify key recommendations and strategies from current clinical guidelines for the management of obesity
- Compare the safety, efficacy, and pharmacokinetic profiles of anti-obesity medications
- Identify best practices for selecting, initiating, and advancing appropriate pharmacological therapies for patient-specific management of obesity

Please complete the pre-activity survey.
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Overview

Obesity and its Consequences

Prevalence of Overweight and Obesity in Adults

- Overweight or obesity affects 69% of adults ≥20 years¹
- Obesity affects ~35% adults ≥20 years¹
- Significant increase in Stage 3 obesity for women²


Obesity Trends among Adults by Gender, Age, Ethnicity. 2005-2014

<table>
<thead>
<tr>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asian American</td>
</tr>
<tr>
<td>Non-Hispanic White</td>
</tr>
<tr>
<td>Latino</td>
</tr>
<tr>
<td>African American</td>
</tr>
<tr>
<td>≥60</td>
</tr>
<tr>
<td>40-59</td>
</tr>
<tr>
<td>20-39</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
</tbody>
</table>


Etiology

Genetic

Heritable traits
Chromosomal abnormalities

Obesogenic Medications

Medications causing weight gain

Environmental

Endocrine disrupting chemicals
Low micronutrient/high calorie foods

Physiologic

Altered microbiome
GLUTs regulation of hunger/satiety hormones

The Complexity of Appetite Regulation

GLP=1 = glucagon-like peptide 1

CCK = cholecystokinin

YY = peptide YY

FFA = free fatty acids

AA = amino acids

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The Complexity of Appetite Regulation

The Physiology of Weight Regain

Overweight and Obesity Classification

Weight-Related Complications of Adiposity

Rationale for Weight Loss

Obesity is a complex, multifactorial, chronic disease

Obesity is associated with a significant increase in mortality and many health risks

The higher the BMI, the greater the risk of morbidity and mortality

[Images and textual content related to appetite regulation, weight regain physiology, overweight and obesity classification, weight-related complications of adiposity, and the rationale for weight loss are included in the document.]

GABA = y-amino butyric acid, AgRP = agouti-related protein, NPY = neuropeptide, αMSH = alpha-melanocyte-stimulating hormone, POMC = pro-opiomelanocortin, CART = cocaine and amphetamine-regulated transcript, MC4R = melanocortin 4 receptor


The Complexity of Appetite Regulation

Adaptive responses to weight loss promote weight regain.
- Fall in energy expenditure
- Increase in appetite
- Dysfunctional hormonal system

Overweight and Obesity Classification

<table>
<thead>
<tr>
<th>Body Mass Index (BMI) in kg/m²</th>
<th>Overweight</th>
<th>Class 1 Obesity</th>
<th>Class 2 Obesity</th>
<th>Class 3 Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-29.9</td>
<td>30-34.9</td>
<td>35-39.9</td>
<td>&gt;40 w/comorbidities</td>
<td></td>
</tr>
</tbody>
</table>

Waist Circumference

Men Abdominal Obesity

Women Abdominal Obesity

>/ = 40 inches (>102 cm)

>/ = 35 inches (>88 cm)

Endocrine Society
Pre-obesity: 26 kg/m²

Weight-Related Complications of Adiposity

- Diabetes risk, metabolic
- Nonalcoholic fatty liver disease and cardiovascular disease mortality
- Urinary stress incontinence
- Asthma
- Osteoarthritis
- Depression

Obesity is associated with a significant increase in mortality and many health risks

The adverse health consequences of increased body fat (especially visceral fat) are not just ‘comorbidities’ or ‘associated risk factors’.

Obesity is defined as a chronic, relapsing, multifactorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissues dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences.

[Images and textual content related to the complexity of appetite regulation, the physiology of weight regain, overweight and obesity classification, weight-related complications of adiposity, and the rationale for weight loss are included in the document.]


Obesity is associated with a significant increase in mortality and many health risks

The higher the BMI, the greater the risk of morbidity and mortality

[Images and textual content related to the complexity of appetite regulation, the physiology of weight regain, overweight and obesity classification, weight-related complications of adiposity, and the rationale for weight loss are included in the document.]

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Clinical Vignette: Evaluation

Meet Pamela

- 42 years old
- Works part-time as a banker
- Lives with her husband and 2 daughters
- Has tried multiple times to lose weight
- Tried phentermine in past for weight loss but did not tolerate the side effects (“felt jittery”)
- Has not reached her weight goal

How would you approach evaluation?

Communication: Using the 5As

Ask
- Permission to discuss weight
- Explore readiness for change

Assess
- BMI, waist circumference, obesity stage
- Explore drivers + complications of excess weight

Advise
- Health risks of obesity + long-term strategies
- Explore + treat obesity-related comorbidities

Agree
- Make plans + targets
- Explore + treat obesity-related comorbidities

Assist
- Identify barriers to optimal health
- Create follow-up plan

Past Medical History + Diagnostics

Sleep Apnea: intermittent use of CPAP
GERD: treated with protonix
Osteoarthritis both knees: takes intermittent ibuprofen
Reproductive barrier: IUD
Mild depression and anxiety: treated successfully with medications
ETOH: drinks socially—1 glass of wine/week. No illicit drugs.

BMI 29 kg/m²
CMP, CBC, LSH noncontributory
TC = 245
HDL = 134
HgbA1C = 5.8
PHQ9 = 4

Pamela’s Perspective

I’ve been overweight since I was 17. I’m always thinking about food, especially sweets and snacks. I find it hard to curb my cravings—instead of eating only a few chips, I usually end up eating the whole bag.

I’ve tried to lose weight many, many times—at least 6 or 7. Sometimes I do lose weight, but I always gain it back again. I’m getting real frustrated.
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Evaluation Summary

Guideline Recommendations

Best Practice Strategies

Guideline Recommendations

Similarities1-3

- Individualized eating plans
- Counseling patients to increase physical activity
- Behavioral interventions
- Medication may be appropriate for some patients
- Referral to an obesity specialist or surgery may be appropriate

Differences1

Endocrine Society paradigm shift toward pharmacologic therapy over no therapy at all for patients:

- With a history of unsuccessful weight loss and maintenance
- Who meet label indications

New Focus

Therapeutic Goals

- Weight loss of 5%-10% of body weight
- Reduce obesity-associated complications within 6 months
- Improve patient health and quality of life

- Reduces CVD risk factors
- Prevents/delays T2DM
- Improves osteoarthritis
- Reduces sleep apnea, depression
- Improves physical function

Guideline-Recommended Comprehensive Lifestyle Therapy*

- Meal Plan: Energy deficit 2500 kcal/day
- Low carb
- Low fat
- Volumetrics
- High protein
- Vegetarian
- Mediterranean DASH

- Physical Activity: Individualized
- Track progress: Daily activity log
- Pedometer logs
- Training metrics

- Behavior: Self-monitoring
- Goal setting
- Education
- Problem-solving strategies
- Stimulus control
- Stress reduction
- Counseling

* Alone or with adjunctive therapies

Clinical Vignette: Evidence Based Management Strategies

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Technology to Support Weight Loss
- Applications to log nutrition and physical activity
- Body-weight scales w/feedback
- Wearable technology
- Websites
- Social media

Next Steps
- Think: Motivational Interviewing & Shared Decision Making
- Explore readiness to change
- Continue lifestyle therapy
- Agree on weight loss goal of 5-7% of Pamela's current weight
- Consensus to discuss medication options

Which therapy would you recommend adding to Pamela's lifestyle plan?
A. Orlistat (Alli, Xenica)
B. Phentermine/topiramate (Qsymia)
C. Naltrexone/bupropion (Contrave)
D. Phentermine (Adipex)
E. Liraglutide (Saxenda)
F. Lorcaserin (Belviq, Belviq XR)

Pharmacologic Therapy
- Therapy Options, Factors to Consider When Selecting Therapy, and Efficacy/Safety Evidence

FDA-Approved Short-Term Anti-Obesity Therapies

<table>
<thead>
<tr>
<th>Generic Drug*</th>
<th>Dose</th>
<th>Contraindications</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine</td>
<td>37.5 mg</td>
<td>Anxiety disorder, CVD, hypertension, MHD, psychiatric, seizures, pregnancy, breastfeeding, drug abuse history</td>
<td>Insomnia, palpitations, dry mouth, taste alterations, diarrhea, tremors, headache, diarrhea, palpitations, vomiting, gastrointestinal distress, anxiety, palpitations, tremors, headache, insomnia, palpitations, tremors, headache</td>
</tr>
<tr>
<td>Dextylpropion</td>
<td>25 or 75 mg</td>
<td>SR</td>
<td>Anxiety disorder, CVD, hypertension, MHD, psychiatric, seizures, pregnancy, breastfeeding, drug abuse history</td>
</tr>
<tr>
<td>Phendimetrazine</td>
<td>75 mg</td>
<td>SR</td>
<td>Anxiety disorder, CVD, hypertension, MHD, psychiatric, seizures, pregnancy, breastfeeding, drug abuse history</td>
</tr>
<tr>
<td>Benphentermine</td>
<td>20-50 mg</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Phentermine
- US Drug Enforcement Agency scheduled drug
  - Risk for addiction
  - Not indicated for long term use
  - 13 weeks by label
- Endocrine Society allows for possible long term use:
  - No CVD
  - No psychiatric/substance abuse history
  - Has been informed about therapies that are approved for long term use
  - Document of label use in patient's medical record
  - No clinical significant increase in pulse/BP when taking phentermine
  - Demonstrates significant weight loss with phentermine
  - Start at 15 or 15 mg/dose and escalate if not achieving significant weight loss
  - Monitor monthly/during dose escalation

*Mechanism of action = Sympathomimetic—noradrenergic, adrenergic, dopaminergic, serotoninergic, histaminergic, cholinergic
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**FDA-Approved Anti-Obesity Therapies**

<table>
<thead>
<tr>
<th>Generic Drug</th>
<th>Mechanism of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat (oral)</td>
<td>Pancreatic lipase inhibitor—impaired gastrointestinal energy absorption, causing excretion of approximately 30% of ingested triglycerides in stool</td>
</tr>
<tr>
<td>Lorcaserin (oral)</td>
<td>Highly selective serotonin 5-HT2C receptor agonist causing appetite suppression</td>
</tr>
<tr>
<td>Phentermine/topiramate ER (oral)</td>
<td>Noradrenergic + GABA-receptor activator, kainite/AMPA glutamate receptor inhibitor causing appetite suppression</td>
</tr>
<tr>
<td>Liraglutide (subcutaneous injection)</td>
<td>GLP-1 receptor agonist</td>
</tr>
<tr>
<td>Naltrexone SR/bupropion (oral)</td>
<td>Opioid receptor antagonist; dopamine and noradrenaline reuptake inhibitor</td>
</tr>
</tbody>
</table>

**Long-Term Efficacy for Anti-Obesity Medications**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Length of Trial</th>
<th>Total Weight Loss</th>
<th>Mean Weight Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat</td>
<td>≥1 year</td>
<td>-5.3 kg</td>
<td>-6.1%</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>1 year</td>
<td>-5.6 kg</td>
<td>-5.8%</td>
</tr>
<tr>
<td>Phentermine/topiramate</td>
<td>≥1 year</td>
<td>-10.2 kg</td>
<td>-9.8%</td>
</tr>
<tr>
<td>Naltrexone/bupropion</td>
<td>≥1 year</td>
<td>-6.1 kg</td>
<td>-5.4%</td>
</tr>
<tr>
<td>Liraglutide*</td>
<td>≥1 year</td>
<td>-8.4 kg</td>
<td>-8.0%</td>
</tr>
</tbody>
</table>

**General Considerations in Pharmacologic Initiation**

- Different patients respond to different medications
  - If one option does not work, consider others
  - Discontinue medication in patients who do not respond with weight loss of at least 5% at 12 weeks
  - Avoid in pregnancy
  - Pregnancy tests at baseline
  - Consider a disclosure signature

**Orlistat**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Frequency</th>
<th>Efficacy</th>
<th>Side Effects</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 mg ODT</td>
<td>120 mg TID within 1 h of meal containing fat</td>
<td>Mean weight loss ranged from 3.9% to 10.2% at year 1 and 17% at year 2 (RCTs 12-week TID)</td>
<td>Diarrhea, cramps, flatulence, fecal urgency, fatty oily stool, increased defecation, fecal incontinence</td>
<td>Chronic malabsorption syndrome, pregnancy, breastfeeding, hypothyroidism, glucocorticoid, use of monoamine oxidase inhibitors, serotonergic 5-HT2C receptor agonist</td>
</tr>
</tbody>
</table>

**Phentermine-Topiramate ER**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Frequency</th>
<th>Efficacy</th>
<th>Side Effects</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>37.5 mg/100 mg</td>
<td>2 tablets twice daily</td>
<td>10% weight loss with treatment vs 2% placebo; increased appetite, fatigue, dizziness, taste alteration, sleep disturbances, anxiety, depression, suicidal thoughts</td>
<td>No significant side effects seen in clinical trials</td>
<td></td>
</tr>
</tbody>
</table>

**Practical Considerations**

- Considerlist of possible multiday options
- Limit fat intake to 30% of calories
- Gastric reflux and diarrhea events

**5 Step Strategy for Therapy Selection**

1. **Patient History**
2. **Safety**
3. **Contraindications**
4. **Side Effects**
5. **Practical Considerations”

**ORCID**

https://orcid.org/0000-0001-5678-9012


- Vilsbøll T, et al. [Journal Name] 2012;344:d7771


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**Liraglutide**

### Dose Frequency
- Weekly by 0.6mg over 5 weeks to target dose of 3.0mg

### Efficacy
- Mean weight loss 9% at 1 year
- Reduced progression to T2DM in patients with prediabetes
- Reduced risk of weight regain at 1 year

### Contraindications
- Medullary thyroid cancer history
- Multiple endocrine neoplasia type 2 history
- History of pancreatitis
- Pregnancy
- Breastfeeding

### Side Effects
- Nausea, vomiting, diarrhea, constipation, hypoglycemia
- Increased lipase
- Increased heart rate
- Nervous system

### Practical Considerations
- Injectable administration
- FDA approved for use in adults with BMI > 25kg/m² or BMI > 27 kg/m² with at least one complication
- Risk Evaluation and Mitigation Strategy

**Lorcaserin**

### Dose Frequency
- 10mg twice daily
- ER 20mg daily

### Efficacy
- Average weight loss 8.5-10%
- Improved cardiovascular risk factors
- Improved HbA1c in patients with T2DM
- Reduced risk in developing T2DM in patients with prediabetes

### Contraindications
- Pregnancy
- Breastfeeding
- Caution with serotonin reuptake inhibitors (due to risk of serotonin syndrome)

### Side Effects
- Headache, dizziness, nausea, dry mouth, cough, and constipation

### Practical Considerations
- Schedule IV Drug
- Effective response to drug
- Independent effect on lowering HbA1c

**Naltrexone-bupropion**

### Dose Frequency
- Initiate 8mg/30mg x 1 week
- Weekly escalation to target dose of 32mg/360mg (2 tablets BMI

### Efficacy
- Weight loss of 8.2% vs 1.4% (placebo)
- Improved cardiometabolic parameters
- Fewer cravings
- Lowered HbA1c in patients with T2DM
- Reduced risk of developing T2DM

### Contraindications
- Uncontrolled hypertension, seizure disorder, anorexia or bulimia, drug or alcohol withdrawal, chronic opioid use, monamine oxidase inhibitors

### Side Effects
- Nausea, constipation, headache, dizziness, vomiting, insomnia, dry mouth
- Transient increase in blood pressure

### Practical Considerations
- Titrate dose on initiation
- Monitor blood pressure
- Monitor closely for depression

**Monitoring Progress**

**Measuring Success**

- Begin therapy with naltrexone-bupropion
- Effective response to therapy
- Improvement in cardiovascular risk factors

- At week 16 (includes titration period) Pamela has lost 2% of her baseline weight and her HbA1c remains 5.8%

- What would be your next management step?

**Ineffective Response to Therapy**

- If no clinical improvement after 12 weeks with one anti-obesity medication, consider:
  - Increasing anti-obesity medication dose, if applicable
  - Alternative anti-obesity medication
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Considerations for Switching Pamela’s Therapy

**Lorcaserin?**
- No history of CVD but borderline high LDL/TC
- Caution w/ SSRI
- Monitor for depression

**Liraglutide?**
- HbA1c remains elevated
- No family history of thyroid or pancreatitis

Maintaining Weight Loss

- Weight regain typically occurs when medication is stopped

Successful weight maintenance includes:
- Self-monitoring
- Weight loss of >3 kg in 4 weeks
- Frequent/regular attendance at weight loss program
- Self-belief that weight can be controlled

Maintaining weight loss is made difficult by the reduction in energy expenditure that weight loss induces


Obesity Specialist Referral—Consultation

- Weight loss <5% at 3 months with approved medication
- Safety or tolerability issues
- Patient-centered concerns

Bariatric Surgery

- BMI ≥ 40 kg/m² if surgical risk is acceptable
- BMI ≥ 35 kg/m² if >1 obesity-related disease
- BMI 30-34.9 kg/m² for T2DM and/or metabolic syndrome
- Inability to achieve + sustain healthy weight loss with prior weight loss efforts

Pamela at Follow-Up with Liraglutide

- Lost 8% baseline weight
- HbA1c = 5.4%
- Sleep apnea is minimal
- No longer requires ibuprofen for osteoarthritis
- Walking 10,000 steps/day, 5 days/week
- Hiking with friends on weekends
- Signed up for a charity 5K

- She has visited 10 times in 6 months for intensive behavioral therapy and monitoring.

At Follow-Up with Liraglutide (cont.)

- Close follow-up
- Continue to prescribe medication with lifestyle
- Pregnancy prevention plan
- Close follow-up
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Key Take Aways

- Obesity is a chronic and often progressive condition
- Obesity management is not about simply reducing numbers on the scale
- Early intervention means addressing root causes and removing roadblocks
- Success is different for every individual
- A patient’s ‘best’ weight may never be an ‘ideal’ weight

NO SHAME, NO BLAME

Reference Section

Please complete the post-activity survey and the activity evaluation.

Efficacy of Lifestyle Intervention

Diabetes Prevention Program

- Multi-center trial in patients with impaired glucose tolerance
- Weight loss of 7% reduced the rate of progression from impaired glucose tolerance to diabetes by 5%
- Reduced risk factors for CVD over 15 years

LOOK AHEAD

- 5145 ethnically diverse overweight/obese adults w/T2DM
- Year 1: 5% weight loss in 68% who received intensive lifestyle counseling vs 13.3% who received usual care
- Year 8: 5% weight loss in 50.5% who received intensive lifestyle counseling vs 35.7% who received usual care

Behavioral Therapy Interventions

- Self-monitoring e.g., food diaries
- Controlling or modifying the stimuli that activate eating
- Slowing down the eating process
- Goal-setting

- Behavioral contracting and reinforcement
- Nutrition education and meal planning
- Modification of physical activity
- Social support
- Cognitive restructuring
- Problem-solving
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**Efficacy of Behavioral Interventions**

- 38 behavioral treatment trials
  - Average baseline BMI: 31.9 kg/m²
  - Overweight adults with 12-26 intervention sessions in year 1 lost 6% baseline weight
  - Control groups lost little or no weight

**Phentermine**

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
<th>Side Effects</th>
<th>Monitoring/Admistration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity, adjunct to comprehensive regimen in management of excessive weight with initial BMI ≥ 30 kg/m² or ≥ 27 kg/m² in presence of other risk factors (eg, diabetes, hypertension, controlled hyperlipidemia)</td>
<td>History of GD, uncontrolled hypertension, during or within 45 days of using MAO inhibitors, glaucoma, pheochromocytoma, pregnancy, breastfeeding, drug abuse or addiction, known or suspected liver disease, obesity associated with any of the following:）、hyperlipidemia, presence of other risk factors (eg, diabetes, hypertension), controlled hyperlipidemia</td>
<td>Nausea, dry mouth, insomnia, headache, dizziness, constipation, loss of appetite, stomach discomfort, palpitations, dizziness, hallucinations, fatigue, tremor, anxiety, depression, increased blood pressure, ischemic events, tachycardia, elevated blood cholesterol</td>
<td>Design should be individualized to elicit an adequate response with the lowest effective dose.</td>
</tr>
</tbody>
</table>

**Orlistat**

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<th>Side Effects</th>
<th>Monitoring/Admistration</th>
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</thead>
<tbody>
<tr>
<td>Obesity management, including weight loss and weight maintenance, when used in conjunction with a reduced calorie diet; to reduce the risk for weight regain after prior weight loss.</td>
<td>Chronic malabsorption syndrome, pregnancy, breastfeeding, cholestasis, some medications (eg, warfarin, antiepileptic agents, levothyroxine, cyclosporine)</td>
<td>Oily spotting, cramps, flatulence with discharge, fatty stools, increased defecation, fecal incontinence, dry mouth</td>
<td>BMI, calorie/fat intake, diarrhea in patients with diarrhea; thyroid function in patient with thyroid disease; liver function test in patients exhibiting symptoms of hepatic impairment; renal function at risk for renal impairment</td>
</tr>
</tbody>
</table>

**Phentermine-Topiramate**

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<th>Side Effects</th>
<th>Monitoring/Administration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjunct to comprehensive regimen in management of excessive weight with initial BMI ≥ 30 kg/m² or ≥ 27 kg/m² in presence of other risk factors (eg, diabetes, hypertension, controlled hyperlipidemia)</td>
<td>Pregnancy and breastfeeding, hyperthyroidism, glaucoma, history of drug allergy, failure within 14 days of taking monoamine oxidase inhibitors</td>
<td>Nausea, dizziness, headache, palpitations, tremor, anxiety, depression, increased blood pressure, ischemic events, tachycardia, elevated blood cholesterol</td>
<td>Naltrexone-bupropion</td>
</tr>
</tbody>
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**Naltrexone-bupropion**

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</thead>
<tbody>
<tr>
<td>Adjunct to reduced calorie diet and increased physical activity for chronic weight management in adults with an initial BMI of 230 kg/m² or ≥ 27 kg/m² in the presence of at least one weight-related comorbid condition (eg, hypertension, type 2 diabetes mellitus, and/or dyslipidemia)</td>
<td>Uncontrolled hypertension, seizure disorder, anorexia or bulimia, drug or alcohol withdrawal, chronic opioid use, monamine oxidase inhibitors</td>
<td>Nausea, constipation, headache, dizziness, vomiting, insomnia, dry mouth, Transient increase in blood pressure</td>
<td>Blood pressure and heart rate; blood glucose; weight; BMI; renal and liver function; mental status for depression, suicidal ideation, anxiety, social functioning, mania, and panic attacks.</td>
</tr>
</tbody>
</table>
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**Lorcaserin**

- **Indications**: Chronic weight management, as an adjunct to a reduced calorie diet and increased physical activity, in adults with an initial BMI of 30 kg/m² or greater, or with an initial BMI of 27 kg/m² and at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes).
- **Contraindications**: Pregnancy, breastfeeding. Caution with serotonergic agents (due to risk of serotonin syndrome).
- **Side Effects**: Avoid in patients with/severe hepatic insufficiency, or renal insufficiency, or severe hepatic insufficiency, or renal insufficiency. Pregnancy, breastfeeding.
- **Monitoring/Admiration**: Weight, waist circumference; CBC, blood glucose (if diabetes); prolactin; depression and/or suicidal thoughts/behavior; signs/symptoms of SS/NMS like peptic ulcer disease (dyspepsia, dependent edema).

**Liraglutide**

- **Indications**: As an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial BMI of 30 kg/m² or greater (obese) or 27 kg/m² or greater (overweight) in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, dyslipidemia).
- **Contraindications**: MODY thyroid cancer history, multiple endocrine neoplasia type 2 history, history of pancreatitis, pregnancy, breastfeeding.
- **Side Effects**: Nausea, vomiting, diarrhea, constipation, hypoglycemia in patients with T2DM, increased isoe, increased heart rate, pancreatitis.

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**Further Considerations in Therapy Selection**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantages</th>
<th>Disadvantages</th>
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</thead>
<tbody>
<tr>
<td>Phenetermine</td>
<td>Inexpensive</td>
<td>Side effect profile</td>
</tr>
<tr>
<td></td>
<td>Weight loss &gt; 3.5%</td>
<td>Long-term data</td>
</tr>
<tr>
<td>Taperimate/phenetermine</td>
<td>Weight loss &gt; 7%</td>
<td>Long-term data</td>
</tr>
<tr>
<td></td>
<td>Inexpensive</td>
<td>Long-term data</td>
</tr>
<tr>
<td>Lorcaserin</td>
<td>Inexpensive</td>
<td>Side effect profile</td>
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<tr>
<td></td>
<td>Weight loss &gt; 7%</td>
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<tr>
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<td>Non-systemic</td>
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<td>Napha/propion</td>
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<td>Food addiction</td>
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<td>Mid-level price range</td>
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<td>Liraglutide</td>
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<td>Injectable</td>
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**References**


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**Table:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenetermine</td>
<td>Inexpensive</td>
<td>Side effect profile</td>
</tr>
<tr>
<td></td>
<td>Weight loss &gt; 3.5%</td>
<td>Long-term data</td>
</tr>
<tr>
<td>Taperimate/phenetermine</td>
<td>Weight loss &gt; 7%</td>
<td>Long-term data</td>
</tr>
<tr>
<td></td>
<td>Inexpensive</td>
<td>Long-term data</td>
</tr>
<tr>
<td>Lorcaserin</td>
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<td>Side effect profile</td>
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</tbody>
</table>
Best Practices in Obesity Management: The Role of New and Emerging Therapies

Reference Section

Without Background

Behavioral Therapy Interventions

- Self-monitoring (e.g., food diaries)
- Controlling or modifying the stimuli that activate eating
- Slowing down the eating process
- Goal-setting

Behavioral contracting and reinforcement
- Nutrition education and meal planning
- Modification of physical activity
- Social support
- Cognitive restructuring
- Problem-solving

Efficacy of Lifestyle Intervention

- Diabetes Prevention Program
  - Multi-center trial in patients with impaired glucose tolerance
  - Weight loss of 7% reduced the rate of progression from impaired glucose tolerance to diabetes by 5%
  - Reduced risk factors for CVD over 15 years

- LOOK AHEAD
  - 5445 ethnically diverse overweight/obese adults w/T2DM
  - Year 1: 5% weight loss in 68% who received intensive lifestyle counseling vs 13.3% who received usual care
  - Year 5: 5% weight loss in 50.5% who received intensive lifestyle counseling vs 35.7% who received usual care

Efficacy of Behavioral Interventions

- 38 behavioral treatment trials
  - Average baseline BMI: 31.9 kg/m²
  - Overweight adults with 12-26 intervention sessions in year 1 lost 6% baseline weight
  - Control groups lost little or no weight

Patient education sessions:
- Healthy diet choices
- Physical activity
- Weight loss goals
- Barriers to weight loss

Regular weight checks
- Peer support

Obesogenic Medications

- Antihistamines
- Steroids
- Hypoglycemic agents
- Estrogens
- Beta blockers
- Calcium channel blockers
- Some antidepressants
- Anticonvulsants/mood stabilizers
- Migraine medications
- Atypical antipsychotics
- HIV medications
- Chemotherapy

Phentermine

- Indications
- Contraindications
- Side Effects
- Monitoring/Administration

Phentermine should be prescribed to attain an adequate response with the lowest effective dose.

The usual adult dose is 3 tablet 10 mg or 4 hour before meals.

Tobacco is screened to facilitate administering one half of the usual dosage for patients not requiring the full dose.

Custom patients should be potential to impose ability to operate machinery or drive a motor vehicle.

Reference:
Best Practices in Obesity Management: The Role of New and Emerging Therapies

**Orlistat**

**Indications**
- Obese management, including weight loss and weight maintenance, when used in conjunction with a reduced-calorie diet to reduce the risk for weight regain after prior weight loss.

**Contraindications**
- Chronic malabsorption syndrome, pregnancy, breastfeeding, cholestasis, some medications (e.g., warfarin, antiepileptic agents, lovastatin, cyclosporine).

**Side Effects**
- Oily spotting, cramps, flatulence with diarrhea, fecal urgency, fatty stools, increased defecation, fecal incontinence.

**Monitoring/Admnistration**
- BMI, calorie/fat intake; serum glucose in patients with thyroid disease; liver function tests in patients exhibiting symptoms of hepatic impairment; renal function in patients at risk for renal impairment.

**Phentermine-Topiramate**

**Indications**
- Adjusted to comprehensive regimen in management of exogenous obesity with an initial BMI of ≥30 kg/m² or ≥27 kg/m² in the presence of at least weight-related comorbidity.

**Contraindications**
- Pregnancy and breastfeeding, hyperthyroidism, glaucoma, when used with 14 days of risk management beta-blockers.

**Side Effects**
- Weight loss, taste alterations, nausea, constipation, dry mouth, elevation in heart rate, memory or cognitive changes.

**Monitoring/Admnistration**
- Before prescribing, hydration status, electrolytes, serum creatinine, symptoms of acute renal, ammonia level in patients with unexplained diarrhea, vomiting or mental status changes; intracranial pressure, suicidality, weight loss, behavior in patients with eating disorder symptoms/risk factors.

**Naltrexone-bupropion**

**Indications**
- Adjunct to a reduced calorie diet and increased physical activity for chronic weight management in adults with an initial BMI of ≥30 kg/m² or ≥27 kg/m² in the presence of at least one weight-related comorbid condition (e.g., hypertension, type 2 diabetes mellitus, and/or dyslipidemia).

**Contraindications**
- Uncontrolled hypertension, severe depression, drug or alcohol withdrawal, chronic opioid use, monamine oxidase inhibitors.

**Side Effects**
- Nausea, constipation, headache, dizziness, vomiting, insomnia, dry mouth.

**Risk Evaluation and Mitigation Strategy**
- Transient increase in blood pressure.

**Lorcaserin**

**Indications**
- Chronic weight management, as an adjunct to a reduced calorie diet and increased physical activity, in adults with either an initial body mass index (BMI) of ≥30 kg/m² or an initial BMI of ≥27 kg/m² and at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, type 2 diabetes).

**Contraindications**
- Pregnancy, breastfeeding, Caution with serotoninergic agents (due to β₂d receptor syndrome).

**Side Effects**
- Avoid in patients w/ T2DM, back pain, cough, hypoglycemia.

**Further Considerations in Therapy Selection**

**Drug**
- Orlistat
- Liraglutide

**Advantages**
- Expensive
- Weight loss 3.5%
- Side effect profile
- No long-term data
- Ineffective
- Long-term data
- Expensive
- Injectable

**Disadvantages**
- Antidepressant
- Teratogen
- Weight loss 3-5%
- Side effect profile
- Food addiction
- Mid-level price range