GHAPP
Gastroenterology & Hepatology Advanced Practice Providers

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Obesity: Pharmacological Management

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Vicki Shah, PA-C, MMS

- Research Support: Gilead, Clinical Area- HCV
- Consultant: AbbVie, Clinical Area- HCV
Why Use Medications?

Objectives:

• Treat diseases
  – Adiposopathy or sick fat disease (SFD)
  – Fat mass disease (FMD)
• Facilitate management of eating behavior
• Slow progression of weight gain/regain
• Improve the health, quality of life, and body weight of the patient with overweight or obesity

Indications

- Patients with obesity (e.g., BMI ≥ 30kg/m²)*
- Patients who are overweight (e.g., BMI ≥ 27kg/m²) with presence of increased adiposity complications (e.g., type 2 diabetes mellitus, hypertension, dyslipidemia)
- Consider pharmacotherapy when diet, exercise, and behavior modification do not produce sufficient weight loss

Considerations

- Variable weight loss over variable duration.
- Average of around 5 – 10% weight loss, with greater weight loss in hyper-responders, and less than 5% weight loss (or even weight gain) in hypo-responders.
- Choice of medication should be tailored to the patient with consideration of co-morbid conditions and DDI
- Assess safety and efficiency every month for 3 months, then every 3 months
- Continue an anti-obesity medication if it is deemed effective and well tolerated.

Considerations

- If no clinical improvement (4 - 5% weight loss) after 12-16 weeks with one anti-obesity medication, then consider
  - Increasing anti-obesity medication dose (if applicable)
  - Giving alternative anti-obesity medication

- If weight loss plateaus, then consider
  - Setting new lower set point?
  - Adding a second medication
  - Increasing physical activity and reviewing diet

Considerations

– Rebound post-treatment: If medication stopped many patients will rebound to a new higher set point

– Treatment course of most studies was around 52 weeks, causing uncertainty in the description of drug rebound trends after 1 year

– When long-term weight loss drugs reached their maximum effects, their drug rebound effects appeared

Phentermine

- Approved in 1959, for short term use 12 wks
- Good candidates: Younger patients who need assistance with appetite suppression
- Do not use: hyperthyroid, uncontrolled HTN, seizure disorder, CVD, glaucoma, drug abuse
- DDI: Monoamine oxidase inhibitors, sympathomimetics, antidepressants, alcohol, adrenergic neuron blocking drugs, and some anesthetic agents

## Phentermine

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism, dosage, and available formulations</th>
<th>Trial and duration</th>
<th>Trial arms</th>
<th>Weight loss (%)</th>
<th>Most common adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine (Adipex-P, Ionamin, Lomaira, Suprenza)</td>
<td>Adrenergic agonist 8–37.5 mg/d Capsule, tablet</td>
<td>Aronne LJ, et al. 28 weeks</td>
<td>15 mg/d 7.5 mg/d Placebo (topiramate ER and phentermine/topiramate ER arms excluded)</td>
<td>6.06a 5.45a 1.71</td>
<td>Dry mouth, insomnia, dizziness, irritability</td>
</tr>
</tbody>
</table>

NOTE: Approved for short-term use

Katherine H. Saunders, MD; Alpana P. Shukla, MD, MRCP; Leon I. Igel, MD; and Louis J. Aronne, MDObesity: When to consider medication OBG Manag. 2018 August;30(8):41-48
Orlistat

- Approved in 1999, take multivitamin daily
- Good candidates: Patients with hypercholesterolemia and/or constipation who can limit their intake of dietary fat
- Do not use: Chronic malabsorption syndrome, cholestasis
- DDI: Cyclosporine, hormone contraceptives, seizure medications, thyroid hormones, warfarin

### Orlistat

<table>
<thead>
<tr>
<th>Medication</th>
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<th>Most common adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat (Alli,20 Xenical21)</td>
<td>Lipase inhibitor 60–120 mg three times per day with meals Capsule</td>
<td>XENDOS22 208 weeks</td>
<td>120 mg three times per day Placebo</td>
<td>9.6 (Week 52)</td>
<td>Fecal urgency, oily stool, flatus with discharge, fecal incontinence</td>
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<td></td>
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<td>5.25 (Week 208)</td>
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<td>5.61 (Week 52)</td>
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<td>2.71 (Week 208)</td>
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</tbody>
</table>
Lorcaserin

- Approved in 2012
- Good candidates: Patients who report inadequate meal satiety
- Do not use: serotonin syndrome, heart failure, psychiatric disorders, and priapism
- DDI: SSRI’s, SNRI’s, MAO inhibitors, anti-dopaminergic medications, St John’s wort, triptans, bupropion, dextromethorphan, CYP 2D6 substrates

Belviq (lorcaserin) [prescribing information]. Zofingen, Switzerland: Arena Pharmaceuticals GmbH.
### Lorcaserin

<table>
<thead>
<tr>
<th>Medication</th>
<th>Mechanism, dosage, and available formulations</th>
<th>Trial and duration</th>
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<th>Most common adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorcaserin (Belviq, Belviq XR)²⁷</td>
<td>Serotonin</td>
<td>BLOOM²⁸ 52 weeks</td>
<td>10 mg twice per day</td>
<td>5.8ᵃ</td>
<td>Headache, dizziness, fatigue, nausea, dry mouth, constipation</td>
</tr>
<tr>
<td>Schedule IV controlled substance</td>
<td>5-HT2C receptor agonist</td>
<td></td>
<td>Placebo</td>
<td>2.2</td>
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<td></td>
<td>10 mg twice per day or 20 mg/d ER Tablet</td>
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<td></td>
<td>BLOSSOM²⁹ 52 weeks</td>
<td>10 mg twice per day</td>
<td>5.8ᵃ</td>
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<td></td>
<td>10 mg/d</td>
<td>4.7ᵃ</td>
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<td></td>
<td></td>
<td>Placebo</td>
<td>2.8</td>
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<tr>
<td></td>
<td></td>
<td>BLOOD-DM³⁰ 52 weeks</td>
<td>10 mg twice per day</td>
<td>4.5ᵃ</td>
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<td>10 mg/d</td>
<td>5.0ᵃ</td>
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<td></td>
<td></td>
<td>Placebo</td>
<td>1.5</td>
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Liraglutide

- Approved in 2014, lower dose 1.8mg used for DM
- Good candidates: Patients who report inadequate meal satiety, and/or have type 2 diabetes, prediabetes, or impaired glucose tolerance; patients requiring use of concomitant psychiatric medications
- Do not use: personal or family hx of medullary thyroid cancer or Type 2 Multiple Endocrine Neoplasia syndrome. Discontinue with suspected pancreatitis, gallbladder disease, or suicidal behavior and ideation
- DDI: May slow gastric emptying

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<tr>
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<tbody>
<tr>
<td>Liraglutide 3 mg (Saxenda)&lt;sup&gt;36&lt;/sup&gt;</td>
<td>GLP-1 receptor agonist 0.6–3 mg/d Prefilled pen for subcutaneous injection</td>
<td>SCALE Obesity and Prediabetes&lt;sup&gt;37&lt;/sup&gt; 56 weeks</td>
<td>3 mg/d Placebo</td>
<td>8.0&lt;sup&gt;a&lt;/sup&gt; 2.6</td>
<td>Nausea, vomiting, diarrhea, constipation, dyspepsia, abdominal pain</td>
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<td></td>
<td>SCALE Diabetes&lt;sup&gt;38&lt;/sup&gt; 56 weeks</td>
<td>3 mg/d 1.8 mg/d Placebo</td>
<td>6&lt;sup&gt;a&lt;/sup&gt; 4.7&lt;sup&gt;a&lt;/sup&gt; 2</td>
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<td>SCALE Maintenance&lt;sup&gt;39&lt;/sup&gt; 56 weeks (after initial ≥5% weight loss with LCD)</td>
<td>3 mg/d Placebo</td>
<td>6.2&lt;sup&gt;a&lt;/sup&gt; 0.2</td>
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</tr>
</tbody>
</table>

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Naltrexone/Bupropion

- Approved in 2014, separately used for addiction or depression/smoking cessation
- Good candidates: Patients who describe cravings for food and/or addictive behaviors related to food; patients who are trying to quit smoking, reduce alcohol intake, and/or have concomitant depression
- Do not use: uncontrolled HTN, seizure disorders, drug/alcohol withdrawal
- DDI: Opioid pain medications, anti-seizure medications, MAO inhibitors

## Naltrexone/Bupropion

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<thead>
<tr>
<th>Medication</th>
<th>Mechanism, dosage, and available formulations</th>
<th>Trial and duration</th>
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<th>Most common adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naltrexone SR/bupropion SR (Contrave)</td>
<td>Opioid receptor antagonist/dopamine and norepinephrine reuptake inhibitor</td>
<td>COR-I&lt;sup&gt;32&lt;/sup&gt; 56 weeks</td>
<td>16/180 mg twice per day</td>
<td>6.1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Nausea, vomiting, constipation, headache, dizziness, insomnia, dry mouth</td>
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<td></td>
<td>COR-II&lt;sup&gt;33&lt;/sup&gt; 56 weeks</td>
<td>8/180 mg twice per day Placebo</td>
<td>5.0&lt;sup&gt;a&lt;/sup&gt;</td>
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<td></td>
<td></td>
<td></td>
<td>Placebo</td>
<td>1.3</td>
<td></td>
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<tr>
<td>Tablet</td>
<td></td>
<td>COR-BMOD&lt;sup&gt;34&lt;/sup&gt; 56 weeks</td>
<td>16/180 mg twice per day Placebo</td>
<td>6.4&lt;sup&gt;a&lt;/sup&gt;</td>
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<td></td>
<td>Placebo</td>
<td>1.2</td>
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<tr>
<td></td>
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<td>COR-DIABETES&lt;sup&gt;35&lt;/sup&gt; 56 weeks</td>
<td>16/180 mg twice per day Placebo</td>
<td>9.3&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Placebo</td>
<td>5.1</td>
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<td></td>
<td></td>
<td></td>
<td>Placebo</td>
<td>5.0&lt;sup&gt;a&lt;/sup&gt;</td>
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<td></td>
<td></td>
<td></td>
<td>Placebo</td>
<td>1.8</td>
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Phentermine/Topiramate

- Approved 2012, topiramate used for seizures and migraine
- Good candidates: Younger patients who need assistance with appetite suppression
- Do not use: glaucoma, uncontrolled HTN, heart disease, or hyperthyroidism. Topiramate can cause birth defects
- DDI: Monoamine oxidase inhibitors. May alter oral contraceptive blood levels

### Phentermine/Topiramate

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</tr>
</thead>
<tbody>
<tr>
<td>Phentermine/topiramate ER (Qsymia)</td>
<td>Adrenergic agonist/neurostabilizer 3.75/23–15/92 mg/d Capsule</td>
<td>EQUIP&lt;sup&gt;24&lt;/sup&gt; 56 weeks</td>
<td>15/92 mg/d 3.75/23 mg/d Placebo</td>
<td>10.9&lt;sup&gt;a&lt;/sup&gt; 5.1&lt;sup&gt;a&lt;/sup&gt; 1.6</td>
<td>Paresthesias, dizziness, dysgeusia, insomnia, constipation, dry mouth</td>
</tr>
<tr>
<td>Schedule IV controlled substance</td>
<td></td>
<td>CONQUER&lt;sup&gt;25&lt;/sup&gt; 56 weeks</td>
<td>15/92 mg/d 7.5/46 mg/d Placebo</td>
<td>9.8&lt;sup&gt;a&lt;/sup&gt; 7.8&lt;sup&gt;a&lt;/sup&gt; 1.2</td>
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<tr>
<td></td>
<td></td>
<td>SEQUEL&lt;sup&gt;26&lt;/sup&gt; 108 weeks (52-week extension of CONQUER trial)</td>
<td>15/92 mg/d 7.5/46 mg/d Placebo</td>
<td>10.5&lt;sup&gt;a&lt;/sup&gt; 9.3&lt;sup&gt;a&lt;/sup&gt; 1.8 (Weeks 0–108)</td>
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</tbody>
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Metformin

• Reduce appetite, effects of GI hormones applicable to weight loss
• Improving insulin sensitivity, leptin sensitivity, reduce neuropeptide Y levels, and increase GLP-1 activity
• 5.8±7.0 kg weight loss with dosage up to 2,500 mg per day
• May help improve: Insulin resistance, PCOS, NAFLD/NASH, CVD, Antipsychotic-related weight gain, HIV protease inhibitor-associated abnormalities (i.e., HIV lipodystrophy), reduce the overall cancer rate and help improve the treatment of multiple cancers

Conclusions

• Weight loss is single most important intervention and requires lifelong monitoring
• 10% weight loss helps with HTN, insulin resistance, hyperlipidemia, OSA, mood in addition to NAFLD/NASH
• Definition from the Obesity Medical Association:
  “Obesity is defined as a chronic, relapsing, multi-factorial, neurobehavioral disease, wherein an increase in body fat promotes adipose tissue dysfunction and abnormal fat mass physical forces, resulting in adverse metabolic, biomechanical, and psychosocial health consequences.”
Thank You

• Special thanks to Dr. Sujit Janardhanan, MD PhD at Rush University with support of Weight Intervention in Liver Disease Clinic