WHAT’S NEW IN OBESITY TREATMENT?
WILL IT MAKE A DIFFERENCE?

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Disclosure

Dr. Ryan has served as an advisor to Nutrisystem and Alere Wellbeing, commercial weight loss programs, to Scientific Intake, a weight loss device company, and the following companies developing medications for obesity management: Arena, Eisai, Novo Nordisk and Vivus.
What’s New?

- In 2012 two new drugs for chronic obesity management were approved by the FDA.

- In 2012 several important papers focused on the potential to produce complete remission of type 2 diabetes with weight loss.
What’s New?

- In 2012 two new drugs for chronic obesity management were approved by the FDA.

- In 2012 several important papers focused on the potential to produce complete remission of type 2 diabetes with weight loss.
How do you think about therapies for obesity?
This is how I think about therapies for obesity...

Self Help Books
Professional Counseling
Group Sessions
Electronic Prompts
Telephone Counseling
Meal Replacements
Liquid Low Cal Diets
Devices for monitoring
Devices for restricting food intake
Weight centric management of chronic meds

Weight loss medications
Surgical Devices
Surgical Gut Re-routing
Will knowledge of weight loss tools make a difference?

- Making a difference will depend on how providers translate efficacy into effectiveness.
Objectives

At the end of the presentation, attendees will be able to

1. describe the safety and efficacy profile of two new medications available for chronic obesity management,

2. discuss the potential for diabetes remission with weight loss and

3. relate the relative efficacy in diabetes remission for different medical and surgical weight loss approaches.
And before we get started....
How much weight do you need to lose?
How much weight loss is needed?

>5% weight loss
- Improvement in risk factors - glucose, insulin, HDL, TG, blood pressure;
- Prevention of diabetes;
- Better glycemic control for persons with T2DM;
- Diabetes and Blood Pressure meds reductions;
- Improvement in urinary stress incontinence, mobility, joint pain, weight-related quality of life, PCOS;

>10% weight loss
- Improvement in sleep apnea

>15% weight loss
- Improvement in cvd mortality and all cause mortality (surgery)

>20% weight loss
- Improvement in LDL cholesterol
Look AHEAD: No difference CV events Intensive Lifestyle Intervention vs. Diabetes Education and Support

- N=5145 subjects with T2DM (half assigned to intensive diet and exercise intervention arm); up to 11 year follow up
- NIH Data and Safety Monitoring Board (DSMB) recommended discontinuation of intensive lifestyle intervention arm, fall 2012
- Although no difference in CV events between arms, other important benefits of lifestyle intervention were seen:
  - Enhanced glycemic control with decreased use of diabetic medications
  - Improved CV risk factors (HDL, TG, BP, CRP)
  - Decreased symptoms of Sleep Apnea
  - Improved mobility
  - Reduced symptoms of urinary stress incontinence
  - Improved symptoms of depression

National institutes of Health. Weight loss does not lower heart disease risk from type 2 diabetes. NIH News; October 2012.
Weight loss and glycemia – CURIOS POWER!
How much weight loss is needed to prevent type 2 diabetes?
How do you explain the curious power of modest weight loss to improve cardiometabolic risk?
Adipose Tissue: Subcutaneous vs Visceral

Weight loss ~ 10%
Loss of visceral AT ~ 30%

Deterioration | Lipid profile | Improvement
---|---|---
Impaired Insulin sensitivity | Improved Blood Insulin | Improved Blood Glucose

<table>
<thead>
<tr>
<th></th>
<th>Risk markers</th>
<th>For thrombosis</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Inflammatory Markers</th>
<th></th>
</tr>
</thead>
</table>

| Impaired | Endothelial Function | Improved |

Increased Risk Low

Abdominal obesity
Increased waist circumference

After weight loss
Reduced waist circumference

Principles in Prevention/Remission of Type 2 Diabetes

Adapted from International Diabetes Center (IDC), Minneapolis, MN.

*IFG=impaired fasting glucose.
Diabetes Remission Definition

American Diabetes Association

- **complete** (normal glycemic measures of at least one year duration with no active pharmacologic therapy or ongoing procedures)
- **partial** (hyperglycemia below diagnostic thresholds for diabetes of at least one year duration with no active pharmacologic therapy or ongoing procedures).
- **prolonged remission** - complete remission of at least five years duration

Proportion of subjects who achieved diabetes remission in the Look AHEAD Study

Year 1
- Intensive Lifestyle (n=2241)
- Diabetes Support, Education (n=2262)

Year 2
- Intensive Lifestyle (n=2241)
- Diabetes Support, Education (n=2262)

Year 3
- Intensive Lifestyle (n=2241)
- Diabetes Support, Education (n=2262)

Gregg EW. JAMA 2012. 308(23): 2489-2496
If modest weight loss has a major impact on diabetes prevention and a modest impact on diabetes remission, what about treatments that produce more weight loss?
# Bariatric Surgery & Diabetes Remission

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Design</th>
<th>BMI range, mean</th>
<th>Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schauer et al. 2012</td>
<td>150</td>
<td>RCT: RYGB vs. Sleeve gastrectomy vs. Medical therapy</td>
<td>27-43, 37</td>
<td>A1c 6% or less without meds</td>
</tr>
<tr>
<td>Mingrone et al, 2012</td>
<td>60</td>
<td>RCT: RYGB vs. BPD vs. Medical therapy</td>
<td>35-? 45</td>
<td>FG &lt;100 and A1c 6.5% or less without meds &gt;1 year</td>
</tr>
<tr>
<td>Cohen et al, 2012</td>
<td>66</td>
<td>Consecutively enrolled observational study of RYGB</td>
<td>30-35</td>
<td>A1c 6.5% or less without meds</td>
</tr>
</tbody>
</table>

### Bariatric Surgery & Diabetes Remission

<table>
<thead>
<tr>
<th>Baseline mean A1c</th>
<th>Design</th>
<th>Follow-up, retention</th>
<th>Results Endpt</th>
<th>Results % loss</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Schauer et al. 2012</strong></td>
<td>9.2±1.5%</td>
<td>RCT: RYGB vs. Sleeve Gastrectomy vs. Medical therapy</td>
<td>12 months, 93%</td>
<td>42% 37% 12%</td>
</tr>
<tr>
<td><strong>Mingrone et al, 2012</strong></td>
<td>8.65±1.5%</td>
<td>RCT: RYGB vs. BPD vs. Medical therapy</td>
<td>2 years, 93%</td>
<td>75% 90% 0%</td>
</tr>
<tr>
<td><strong>Cohen et al, 2012</strong></td>
<td>9.7+1.5%</td>
<td>Consecutively enrolled observational study of RYGB</td>
<td>up to 6 years, med = 5 y, 100%</td>
<td>88%</td>
</tr>
</tbody>
</table>

# Bariatric Surgery & Diabetes Remission

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean duration T2DM</th>
<th>Design</th>
<th>Response correlations</th>
<th>Adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schauer et al. 2012</td>
<td>~8.7 ± 5.5 years</td>
<td>RCT: RYGB vs. Sleeve Gastrectomy vs. Medical therapy</td>
<td>Surgery vs. Medical; not by procedure</td>
<td>Reoperation 3, Reoperation 1</td>
</tr>
<tr>
<td>Mingrone et al, 2012</td>
<td>~6 ± 1 year</td>
<td>RCT: RYGB vs. BPD vs. Medical therapy</td>
<td>Not age, sex, baseline BMI, duration diabetes</td>
<td>Reoperation 1, Reoperation 1</td>
</tr>
<tr>
<td>Cohen et al, 2012</td>
<td>12.5 ± 7.4 years</td>
<td>Consecutively enrolled observational study or RYGB</td>
<td>No predictors identified</td>
<td>No major complications, 15% minor complications</td>
</tr>
</tbody>
</table>

The Longitudinal Assessment of Bariatric Surgery (LABS) Study

4776 patients in 10 United States Centers 2005-2007

<table>
<thead>
<tr>
<th></th>
<th>Lap Band</th>
<th>Lap Roux-en-Y</th>
<th>Open Roux-en-Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>1198</td>
<td>2975</td>
<td>437</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>46 ± 12.5</td>
<td>43.6 ± 11</td>
<td>45.9 ± 10.7</td>
</tr>
<tr>
<td>BMI (median)</td>
<td>44.1</td>
<td>46.9</td>
<td>50.9</td>
</tr>
<tr>
<td>Death in 30 days</td>
<td>0</td>
<td>6 (0.2)</td>
<td>9 (2.1)</td>
</tr>
<tr>
<td>DVT</td>
<td>3 (0.3)</td>
<td>12 (0.4)</td>
<td>5 (1.1)</td>
</tr>
<tr>
<td>Failure to be discharged in 30 days</td>
<td>0</td>
<td>13 (0.4)</td>
<td>4 (0.9)</td>
</tr>
<tr>
<td>Composite endpoint* in 30 days</td>
<td>12 (1.0)</td>
<td>143 (4.8)</td>
<td>34 (7.9)</td>
</tr>
</tbody>
</table>

*Composite endpoint: death, DVT or venous thromboembolism, intervention or failure to be discharged within 30 days

Objectives

At the end of the presentation, attendees will be able to

1. describe the safety and efficacy profile of two new medications available for chronic obesity management,

2. discuss the potential for diabetes remission with weight loss and

3. relate the relative efficacy in diabetes remission for different medical and surgical weight loss approaches.
The treatment gap

Diet and Exercise

Surgery and Surgical Devices
Medications support adherence to dieting behaviors

- Medications that act centrally target:
  - Hunger
  - Satiety
  - Craving

- Medications (orlistat) can block fat absorption
Principles of Prescribing for Weight Loss

- Medications work through hunger and satiety control, but they don’t work without the intention to diet.
- Skills training in lifestyle change is foundational… diet, physical activity and behavior modification.
- Not all patients respond. Usually, 12 weeks should produce at least 3% weight loss and we want 5% at 6 months.
- Plateau in weight usually occurs after 6 months.
- Treatments work if they are used. Prescribe chronically.
# Medications available before 2012

<table>
<thead>
<tr>
<th>Agent</th>
<th>PHENTERMINE</th>
<th>ORLISTAT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mechanism</strong></td>
<td>Central Noradrenergic</td>
<td>Peripheral Pancreatic lipase inhibitor</td>
</tr>
<tr>
<td><strong>Approval</strong></td>
<td>Short-term use Class IV</td>
<td>Long-term use Not scheduled Also available OTC</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>$</td>
<td>$$$</td>
</tr>
</tbody>
</table>
| **Common Adverse Effects** | • Restlessness  
                   • Insomnia  
                   • Increase in pulse  
                   • Increase in blood pressure | • GI symptoms including oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, and others less frequently  
                   • Increase in urinary oxalate |

Recently Approved Pharmacotherapy

<table>
<thead>
<tr>
<th>Agent</th>
<th>Phentermine/topiramate ER(^1,2) Qsymia™</th>
<th>Lorcaserin(^3,4) Belviq®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Status</td>
<td>Approved July 2012</td>
<td>Approved June 2012</td>
</tr>
<tr>
<td>Mechanism</td>
<td>PHEN stimulates norepinephrine release from hypothalamic neurons; TPM is an anticonvulsant</td>
<td>Selectively targets the 5-HT2C receptor</td>
</tr>
<tr>
<td>Follow-up Duration</td>
<td>56 (108*) weeks</td>
<td>52 (104*) weeks</td>
</tr>
<tr>
<td>Common Adverse Effects</td>
<td>• Dry mouth</td>
<td>• Headache</td>
</tr>
<tr>
<td></td>
<td>• Tingling</td>
<td>• Dizziness</td>
</tr>
<tr>
<td></td>
<td>• Constipation</td>
<td>• Nausea</td>
</tr>
<tr>
<td></td>
<td>• Altered taste sensation</td>
<td>*2 year extension data available</td>
</tr>
<tr>
<td></td>
<td>• Upper respiratory infection</td>
<td></td>
</tr>
</tbody>
</table>

Let’s first look at Phentermine/Topiramate ER.
Phentermine/Topiramate ER

- Once-a-day, oral, extended release topiramate
- Low doses of previously approved medications to minimize side effects

DOSING:
1. Begin with low dose for 2 weeks: phentermine 3.75/ topiramate 23
2. Advance to treatment dose: phentermine 7.5/ topiramate 46
3. If <3% weight loss after 12 weeks, either discontinue or advance to full dose: phentermine 15/ topiramate 92 (transition dose: phentermine 11.25/ topiramate 69 for 2 weeks)
4. If <5% weight loss after 12 weeks on full dose, then discontinue (take every other day for one week)
Weight Change Over 2 Years With Phentermine/Topiramate ER


Data are shown with least squares mean (95% CI).

Completers Population

<table>
<thead>
<tr>
<th></th>
<th>Placebo n:</th>
<th>PHEN/TPM CR 7.5/46 n:</th>
<th>PHEN/TPM CR 15/92 n:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks</td>
<td>0</td>
<td>104</td>
<td>108</td>
</tr>
<tr>
<td></td>
<td>227</td>
<td>197</td>
<td>248</td>
</tr>
<tr>
<td></td>
<td>227</td>
<td>227</td>
<td>295</td>
</tr>
<tr>
<td></td>
<td>227</td>
<td>153</td>
<td>153</td>
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<tr>
<td></td>
<td>227</td>
<td>153</td>
<td>295</td>
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<tr>
<td></td>
<td>227</td>
<td>152</td>
<td>295</td>
</tr>
<tr>
<td></td>
<td>208</td>
<td>137</td>
<td>295</td>
</tr>
<tr>
<td></td>
<td>-10.5% ITT-LOCF</td>
<td>-9.3% ITT-LOCF</td>
<td>-9.3% ITT-LOCF</td>
</tr>
<tr>
<td></td>
<td>-10.7% for Cs</td>
<td>-2.2% for Cs</td>
<td>-1.8% for Cs</td>
</tr>
</tbody>
</table>

Qsymia™
Effect of Phentermine/Topiramate ER on Blood Pressure and Lipid Levels After 56 Weeks

Data are presented from the intention-to-treat analysis with LOCF. Least-squares means ± 95% CI

*P<0.05

All P values are vs placebo.

Effects of Phentermine/Topiramate ER in Patients with T2DM: 2 years of treatment

Change in A1C

<table>
<thead>
<tr>
<th>Group</th>
<th>Baseline Mean A1C %</th>
<th>Placebo (n=55)</th>
<th>Phen/Top 7.5/46 mg (n=26)</th>
<th>Phen/Top 15/92 mg (n=64)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Mean A1C (%)</td>
<td>6.9</td>
<td>7.3</td>
<td>6.9</td>
<td></td>
</tr>
<tr>
<td>LS Mean ΔA1C (%)</td>
<td>-0.04</td>
<td>-0.42</td>
<td>-0.23</td>
<td></td>
</tr>
</tbody>
</table>

- Percent increase minus percent decrease.

Change in Diabetes Medications

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients With Net Change* in Diabetes Medications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (n=227)</td>
<td>7.1</td>
</tr>
<tr>
<td>Phen/Top 7.5/46 mg (n=153)</td>
<td>1.9</td>
</tr>
<tr>
<td>Phen/Top 15/92 mg (n=295)</td>
<td>0</td>
</tr>
</tbody>
</table>

* Percent increase minus percent decrease.
‡ P=0.013 for between-group differences.

# Phentermine/Topiramate ER Safety Data

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Placebo (%) (n=993)</th>
<th>PHEN/TPM ER 7.5/46 (%) (n=498)</th>
<th>( P ) Value</th>
<th>PHEN/TPM ER 15/92 (%) (n=994)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth</td>
<td>2</td>
<td>13</td>
<td>&lt;0.0001</td>
<td>21</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Paraesthesia</td>
<td>2</td>
<td>14</td>
<td>&lt;0.0001</td>
<td>21</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Constipation</td>
<td>6</td>
<td>15</td>
<td>&lt;0.0001</td>
<td>17</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>1</td>
<td>7</td>
<td>&lt;0.0001</td>
<td>10</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Insomnia</td>
<td>5</td>
<td>6</td>
<td>0.3832</td>
<td>10</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3</td>
<td>7</td>
<td>0.0005</td>
<td>10</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Back pain</td>
<td>5</td>
<td>6</td>
<td>0.6199</td>
<td>7</td>
<td>0.0386</td>
</tr>
<tr>
<td>Nausea</td>
<td>4</td>
<td>4</td>
<td>0.6754</td>
<td>7</td>
<td>0.0139</td>
</tr>
<tr>
<td>Blurred vision</td>
<td>4</td>
<td>4</td>
<td>0.7729</td>
<td>6</td>
<td>0.0157</td>
</tr>
</tbody>
</table>

Phentermine/Topiramate ER REMS Program

- FDA Pregnancy Category X
  - Topiramate monotherapy for epilepsy in pregnancy associated with 2- to 5-fold increased prevalence of oral clefts
- Risk Evaluation and Mitigation Strategy (REMS)
  - Inform patients about increased risk of orofacial clefts, in infants exposed to phentermine/topiramate during the first trimester of pregnancy
  - Importance of contraception in women of child-bearing potential, pregnancy checks, and need to discontinue phentermine/topiramate immediately if pregnancy occurs
- Distribution will change from mail order to certified retail pharmacies in June, 2013.

Phentermine/Topiramate ER

**Mechanism of Action**

- **Phentermine:**
  - Sympathomimetic amine, NE release
  - Blunts appetite
- **Topiramate ER:**
  - Increases GABA activity, antagonize AMPA/ kainate glutamate receptor, carbonic anhydrase inhibitor
  - Prolongs satiety

**Indications and Dose**

- Approved by FDA, July 2012, schedule IV
- **Indication:**
  - Weight loss in patients with BMI ≥30 kg/m² or BMI ≥27 kg/m² with weight-related co-morbid condition(s)
- **Treatment dose daily:**
  - phentermine 7.5 mg
  - topiramate ER 46 mg
- **Max dose daily:**
  - phentermine 15 mg
  - topiramate ER 92 mg

**Contraindications and Warnings**

- **Contraindications:**
  - Pregnancy, glaucoma, hyperthyroidism, MAOIs
- **Warnings:**
  - Fetal toxicity
  - Increased heart rate
  - Suicide and mood and sleep disorders
  - Acute myopia and glaucoma
  - Cognitive impairment
  - Metabolic acidosis
  - Creatinine elevations
  - Hypoglycemia with diabetes meds

Let’s look at lorrcaserin.
Lorcaserin

- Dosage is 10 mg BID
- Developed as a specific 5HT 2c receptor agonist to avoid 5HT 2b receptors on the heart valves.
- Fenfluramine & dexfenfluramine were popular weight loss medications removed from the market in 1997 because of heart valve problems.
Weight Change With Lorcaserin Over 2 Years (ITT-LOCF Population)*

*Only included patients who continued the study past year 1

Effect of Lorcaserin on Metabolic Measures in Obese Adults After 1 Year

Effect of Lorcaserin in Patients with T2DM: BLOOM-DM Study

Change in HbA1C

Baseline Mean A1C (%)

Placebo (n=248) 8.0
Lorcaserin 10 mg BID (n=251) 8.1
Lorcaserin 10 mg QD (n=93) 8.1

LS Mean ΔA1C (%)

-0.4
-0.9 *
-1 *

*P<0.001 vs placebo.
†P=0.087 vs placebo.

Decreasing Use in Diabetes Medications

Patients Decreasing Use of Antidiabetic Agents (%)

Placebo (n=248)
Lorcaserin 10 mg BID (n=251)
Lorcaserin 10 mg QD (n=95)

-11.7
-17.1 †
-23.4 †
## Lorcaserin Safety Data

<table>
<thead>
<tr>
<th>Common Event</th>
<th>Lorcaserin 10 mg BID n=1593, Year 1 n (%)</th>
<th>Lorcaserin 10 mg BID n=573, Years 1 and 2 n (%)</th>
<th>Placebo n=1584, Year 1 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>287 (18.0)</td>
<td>41 (7.2)</td>
<td>175 (11.0)</td>
</tr>
<tr>
<td>Upper respiratory infection</td>
<td>235 (14.8)</td>
<td>83 (14.5)</td>
<td>189 (11.9)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>213 (13.4)</td>
<td>94 (16.4)</td>
<td>190 (12.0)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>130 (8.2)</td>
<td>10 (1.7)</td>
<td>60 (3.8)</td>
</tr>
<tr>
<td>Nausea</td>
<td>119 (7.5)</td>
<td>20 (3.5)</td>
<td>85 (5.4)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>114 (7.2)</td>
<td>49 (8.6)</td>
<td>130 (8.2)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>109 (6.8)</td>
<td>34 (5.9)</td>
<td>85 (5.4)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>106 (6.7)</td>
<td>41 (7.2)</td>
<td>96 (6.1)</td>
</tr>
<tr>
<td>Constipation</td>
<td>106 (6.7)</td>
<td>14 (2.4)</td>
<td>64 (4.0)</td>
</tr>
<tr>
<td>Back pain</td>
<td>99 (6.2)</td>
<td>34 (5.9)</td>
<td>89 (5.6)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>95 (6.0)</td>
<td>15 (2.6)</td>
<td>48 (3.0)</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>83 (5.2)</td>
<td>1 (0.2)</td>
<td>37 (2.3)</td>
</tr>
<tr>
<td>Gastroenteritis (viral cause)</td>
<td>79 (5.0)</td>
<td>18 (3.1)</td>
<td>64 (4.0)</td>
</tr>
<tr>
<td>Influenza</td>
<td>73 (4.6)</td>
<td>38 (6.6)</td>
<td>69 (4.4)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>70 (4.4)</td>
<td>38 (6.6)</td>
<td>75 (4.7)</td>
</tr>
</tbody>
</table>

Lorcaserin Warnings

- Lorcaserin is contraindicated in pregnancy
- Warnings:
  - Should not be used in patients who are taking SSRIs or SNRIs, TCAs, triptans and tryptophan

SSRI=selective serotonin reuptake inhibitor. SNRI=selective serotonin-norepinephrine reuptake inhibitor. TCA=tricyclic antidepressant
## Lorcaserin

### Mechanism of Action
- Selective 5-HT2C receptor agonist
- Stimulates α-MSH production from POMC neurons resulting in activation of MC4R
- Increases satiety

### Indications and Dose
- **Approved by FDA**
  - June 2012
- **Indication:**
  - Weight loss in patients with BMI ≥30 kg/m² or BMI ≥27 kg/m² with weight-related co-morbid condition(s)
- 10 mg po bid, schedule pending (IV)
- Discontinue if 5% weight loss is not achieved in 12 wks

### Warnings and Contraindications
- **Contraindications:**
  - Pregnancy
- **Warnings:**
  - Coadministration with other serotonergic or antidopaminergic agents
  - Valvular heart disease
  - Cognitive impairment
  - Psychiatric disorders (euphoria, suicidal thoughts, depression)
  - Priapism
  - Risk of hypoglycemia with diabetes meds

<table>
<thead>
<tr>
<th>Agent</th>
<th>Naltrexone/BupSR(^1)</th>
<th>Liraglutide(^2,3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approval Status</td>
<td>FDA requested additional Phase 3 data</td>
<td>In Phase 3 clinical trials</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Naltrexone, opioid receptor antagonist; Bup, norepinephrine-dopamine reuptake inhibitor</td>
<td>Glucagonlike peptide-1 analogue</td>
</tr>
<tr>
<td>Follow-up Duration</td>
<td>56 weeks</td>
<td>56 weeks</td>
</tr>
</tbody>
</table>
| Common AEs     | • Nausea  
                • Headache  
                • Constipation  
                • Dizziness  
                • Vomiting  
                • Dry mouth | • Nausea  
                • Vomiting  
                • Gastro-intestinal effects |

Will these medications make a difference?

- Yes, they can.
- The new medications can help more people achieve more weight loss than with diet and exercise alone.
- But we are not at a point yet where we can “treat to goal”.
Providers need...

- **Tools**
  - Drugs, Devices, Diet and Exercise Aids
  - Systems approach – protocols for office

- **Training**
  - Pre-graduate education
  - Certification
  - CME

- **Incentives and Reinforcement**
These new drugs are tools in YOUR toolbox, too.

- Self Help Books
- Professional counseling
- Group Sessions
- Electronic Prompts
- Telephone Counseling
- Meal Replacements
- LCD, Liquid Devices for monitoring
- Devices for restricting food intake
- Weight centric management of chronic meds
- **Weight loss medications**
- Surgical Devices
- Surgical Gut Re-routing
Thank You

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