Anti-Obesity Medications: Optimizing Successful Obesity Treatment

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ABC’s: Affiliations/Background/Conflicts

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Master’s Degrees:
- Exercise Physiology
- Public Health and Physical Activity

Disclosures
- Novo Nordisk – Consultant/Speaker
- Orexigen – Consultant/Speaker
Road Map

- Anti-Obesity Medications
- Individualized Care for our Patients
- Anti-Obesity Medicine (AOM’s) Questions
- Coverage
Obesities

Intervention Clusters

Isolated Therapies in Obesity

Is comprehensive treatment important or just ideal?

Additive Effects of:
- Behavior Therapy
- Meal Replacements
- Pharmacotherapy

Weight Loss (%)

Time/Months

Wadden, Arch Int Med. 2001;161:218
Pharmacotherapy is an integral treatment modality and should be considered at every stage of the disease treatment.
Am I a candidate for anti-obesity medication?

FDA

- For patients with BMI > 30
- For patients with BMI > 27 or above with concomitant risk factors or diseases (hypertension, dyslipidemia, CHD, type 2 diabetes, sleep apnea)
- To be used as an adjunct to intensive lifestyle intervention for nutrition, physical activity, and behavior modification.
What Anti-Obesity Medications are available today?

- Sympathomimetics
  - Phentermine
  - Diethylpropion
  - Phendimetrazine
- Phentermine / Topiramate
- Lorcaserin
- Naltrexone / Bupropion
- Liraglutide
- Orlistat
Medication “NTK” List

• Mechanisms: Known and Unknown
• Side Effects Vary Widely
• Not widely covered by insurance
• Cost variation
• FDA: Discontinue, Increase dose, or and consider alternate therapy if 4-5% weight loss not achieved by 3 months at full dose.
Does Early Good Response Make a Difference?

Those who lost ≥ 4.5% total body weight by week 12 went on to lose 10%

<table>
<thead>
<tr>
<th>MITT Lorcaserin BID</th>
<th>Week 12</th>
<th>Completed Week 12</th>
<th>Completed Week 52</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 3097</td>
<td>≥4.5% wt loss</td>
<td>1369/3097 (44.2%)</td>
<td>1083/1369 (79.1%)</td>
</tr>
<tr>
<td></td>
<td>&lt;4.5% wt loss</td>
<td>1168/3097 (37.7%)</td>
<td>680/1168 (58.2%)</td>
</tr>
</tbody>
</table>

Slide Courtesy of Dr. Steve Smith
Why can’t I just take my meds doc? Naltrexone/Bupropion
How long will I be on medication?

Smith et al NEJM 2010
What if I have already lost some weight?

Run in = 6% weight loss
Treatment = 6% additional weight loss
>5% weight loss maint. 81% vs. 49%
>5% additional wt loss 51% vs 22%

Follow-up
Med Withdrawal = 4.1% loss maintained vs 0.3% gain

Can I take AOM’s if I had a bariatric surgery or an intermediate procedure?
Post-Bariatric Surgery Weight Regain & Short-term Liraglutide

- Small study N=15
- Excess Wt loss <50% after surgical follow-up or regained weight more than 15% of weight nadir.
- Avg wt regain was 14kg.
- Avg of 7.4kg loss on liraglutide.

Phentermine: Retrospective Data, NEEDS RCT for comparable data.

Diet, Exercise & Phentermine

Diet & Exercise

What would the Ideal Anti-Obesity Agent look like?

- Decrease hunger or increase satiety
- Decrease Cravings
- Stimulate thermogenesis
- Produce fat loss
- Preserve skeletal muscle mass
- Decrease muscle efficiency
- No significant side effects
- Safe for long term use
- No abuse potential
- Affordable
Will my anti-obesity medication be covered by my insurance?

- Initiation Criteria
- “Generics”
- Continuation Criteria
- Polypharmacy
- Maintenance
- Relapse
Is there a medicine that can help me with my weight doctor?

Approximately 100 million Americans are overweight or obese
- 60% are engaged in weight-loss activities
- 2% are on prescription therapy

2011 Prevalence
N=238 MM

N=106 MM

N=67 MM

N=60 MM

N=2.1 MM

Body Mass Index (BMI) 27-29.9 + 1 Comorbidity\(^a\) or BMI ≥30
(27 MM)

(79 MM)

(NHANES)

Patients Classified As Overweight/Obese By Physician\(^b\)
(NHANES)

Engaged in Diet and/or Exercise
Trinity PMR 2012 data – patient survey:
Q: Are you currently dieting and/or exercising to lose weight?
A: 90% are at least using diet/exercise

On Rx Therapy
(IMS 2011 data)

Note: Size of boxes not drawn to scale.
\(^a\)Includes diabetes; \(^b\)Represents patients who have been told by their physician that they are overweight.
NHANES=National Health and Nutrition Examination Survey.
What will trigger the discussion?
Challenges and Patient Fears Seen & Unseen
What does “Health” look like?
### Weight Loss: 1 and 2 Year Responder Rates

<table>
<thead>
<tr>
<th>Weight Loss</th>
<th>≥ 5%</th>
<th>≥10%</th>
<th>≥15%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phentermine 1 yr*</td>
<td>97%</td>
<td>83%</td>
<td>62%</td>
</tr>
<tr>
<td>Phentermine 2 yr*</td>
<td>89%</td>
<td>65%</td>
<td>15%</td>
</tr>
<tr>
<td>Qsymia 1 yr</td>
<td></td>
<td>47%</td>
<td>30%</td>
</tr>
<tr>
<td>Belviq 1 yr</td>
<td>47%</td>
<td>23%</td>
<td></td>
</tr>
<tr>
<td>Contrave 1 yr</td>
<td>67%</td>
<td>36%</td>
<td>13%</td>
</tr>
<tr>
<td>Saxenda 1 yr</td>
<td>62%</td>
<td>34%</td>
<td></td>
</tr>
</tbody>
</table>

* Used with low carbohydrate ketogenic diet

Phentermine – Hendricks 2011; Qsymia & Belviq – Yanovski 2014; Contrave – Apovian 2013
Comparative Expected Weight Loss

![Bar chart showing average placebo-subtracted weight loss (%) for different medications.](chart.png)

- Qlsta: 3.1%
- Liitrac: 3.2%
- Liraglutide: 4.0%
- Tesofensine: 5.0%
- Bupropion: 7.4%
- Bupropion-Zonisamide: 7.2%
- Didex 50: 9.8%

Average placebo-subtracted weight loss (%)
Sympathomimetics/Phentermine

TYPICAL DOSAGE RANGE 15-37.5 MG

WEIGHT LOSS (LBS)

PHENTERMINE
ALTERNATE EVERY MONTH
PLACEBO

MONTHS

Combination Phentermine / Topiramate

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Qsymia®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Loss</td>
<td>12.8% at 1 year; 11.5% at 2 years DEA Schedule IV</td>
</tr>
<tr>
<td>Dose</td>
<td>Recommended dose: 7.5/46mg (phentermine/topiramate) Maximum dose: 15/92 mg/day</td>
</tr>
<tr>
<td>Mechanism of Action</td>
<td>Unknown; thought to improve satiety; cravings may diminish</td>
</tr>
<tr>
<td>Responder Rates 1 Year</td>
<td>≥10% loss: 47%</td>
</tr>
<tr>
<td>Adverse Events</td>
<td>Typical for each drug (phentermine and topiramate)</td>
</tr>
</tbody>
</table>

Garvey WT, Expert Opin Drug Saf. 2013
Qsymia Package Insert, 2015
<table>
<thead>
<tr>
<th>Trade Name</th>
<th>BELVIQ®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Loss</td>
<td>4% at 1 year, 10% if ≥ 4.5% at 3 months</td>
</tr>
<tr>
<td>Dose</td>
<td>20 mg/d (one tablet 10 mg twice daily) DEA Schedule IV</td>
</tr>
<tr>
<td>Mechanism of Action</td>
<td>Serotonin (5-HT)2C receptor agonist in pro-opiomelanocortin (POMC) neurons in hypothalamic arcuate nucleus</td>
</tr>
<tr>
<td>Responder Rates 1 Year</td>
<td>≥10% wt. loss: 23%</td>
</tr>
<tr>
<td>Adverse Events</td>
<td>Headache 27%, nausea 11%, dizziness 8%, no serious ASES side effects. Pregnancy Category X</td>
</tr>
</tbody>
</table>

**Caution for concomitant use with other drugs that effect serotonin**
Combination Bupropion/Naltrexone

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>CONTRAVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Loss</td>
<td>4%, 8% Completer data, 12% AOM+BMOD Completer at 1 year Unscheduled</td>
</tr>
<tr>
<td>Dose</td>
<td>Maximum dosage: 32 mg/360 mg per day (two tablets twice daily)</td>
</tr>
<tr>
<td>Mechanism of Action</td>
<td>Dual, bupropion activates pro-opiomelanocortin neurons, Naltrexone inhibits opioid antagonism on these POMC neurons.</td>
</tr>
<tr>
<td>Responder Rates 1 Year</td>
<td>≥10% wt. loss: 39%</td>
</tr>
<tr>
<td>Adverse events</td>
<td>Nausea 32%, constipation, headache, no serious ASEs.</td>
</tr>
</tbody>
</table>

**Warnings: depression/suicidal thoughts; seizures, hepatotoxicity, elevated blood pressure**

Apovian C. 2013
CONTRAVE Package Insert, 2015
**Liraglutide**

<table>
<thead>
<tr>
<th>Trade Name</th>
<th>Saxenda (Specifically for obesity treatment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Loss</td>
<td>4.4% at 1 year, 6% Completer data Unscheduled</td>
</tr>
<tr>
<td>Dose</td>
<td>5 week titration, 3.0mg SQ daily</td>
</tr>
<tr>
<td>Mechanism of Action</td>
<td>Glucagon-like-peptide -1 (GLP-1) receptor agonist; satiety, delays gastric emptying</td>
</tr>
<tr>
<td>Responder Rates 1 year</td>
<td>≥10% wt. loss: 34%, &gt;/= 5% 62%</td>
</tr>
<tr>
<td>Adverse Events</td>
<td>nausea (39%), diarrhea (21%), constipation (19%)</td>
</tr>
</tbody>
</table>

**Black Box warnings for rare occurrences of pancreatitis, and has been associated with medullary thyroid carcinoma in rats and mice. Do not use with MENS type 2**