Disclosures

- The Western Multi-State Division is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center’s Commission on Accreditation.
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Pharmacological Treatment of Obesity

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JORDAN VALLEY MEDICAL CENTER
I have not conflict of interest to declare
I am board certified in Endocrinologist and in Internal Medicine
I am a Certified Diabetes Educator
I work Through Physicians Group of Utah at Jordan Valley Medical Center
Definition of Obesity

BMI = Weight (kg) / Height (m²)

Asians:
- Overweight = BMI 23-27.4
- Obesity = BMI ≥27.5
- Morbid Obesity = BMI ≥37.5

Non-Asians:
- Overweight = BMI 25-29.9
- Obesity = BMI ≥30
- Morbid Obesity = BMI ≥40
Rates of Obesity in the U.S.A.

2/3 of the US population is overweight

1/3 of the US population is obese

36% of those living in US, about 78 million people in US, are estimated to be obese with a BMI >30 kg/m²

No state had a prevalence of obesity less than 20%

2 states (Mississippi and West Virginia) had a prevalence of obesity of 35% or greater
POTENTIAL CONTRIBUTORS TO OBESITY

Inside the Person

- Disordered Eating (night eating syndrome, binge eating, “food addiction”)
- Emotional Coping
- Hyper-reactivity to Environmental Food Cues
- Delayed Satiety
- Heightened Hunger Response

Outside the Person

- Environmental/Chemical Toxins
- Increased Availability of Energy Dense, Nutrient Poor Foods & Beverages
- Larger Portion Sizes
- Skipping Meals
- Food Insecurity
- Market Economy
- Food Surplus
- Pervasive Food Advertising

Contributors to Energy Storage

- Increased Intake
- Maternal Employment
- Breast Feeding and/or Related Factors
- Maternal Stress
- Maternal Smoking
- Maternal Obesity
- Delayed Prenatal Care
- Birth Order (first-born in family)
- Having Children (for women)
- Non-parental Childcare
- Maternal Over-nutrition During Pregnancy
- Weight Gain Inducing Drugs
- Smoking Cessation
- Sleep Deficits

- Intake & Expenditure (Or Unknown)
- Family Conflict
- Social Networks
- Lack of Employer Preparedness to Assist with Obesity
- Westernization & Economic Development
- Low SES & Nutrition Support
- Living in Crime-prone Areas
- Weight Cycling (yo-yo dieting)

- Decreased Expenditure
- Consistent Temperature (i.e. air conditioning/heating, thermoregulation)
- Increased Sedentary Time (i.e. inactive leisure “screen” time, inactive job requirements)
- Built Environment (i.e. stairwell design/access, building design, absence of or poor sidewalks)
- Decreased Opportunity for Non-exercised Based Physical Activity (i.e. driving vs. walking to work and school, sedentary jobs)

Contributor/Influencer

- Environmental Pressures on Physical Activity
- Biological/Medical
- Maternal Developmental
- Economic
- Food and Beverage Behavior/Environment
- Psychological
- Social

* Potential contributors indicate anything that has been put forth in the research literature as a question of investigation and is not intended to be a verification of whether or not, or the extent to which, each may or may not contribute.
Medical Complications of Obesity

Patients with a BMI 30-35 have decreased life expectancy by 2-4 yrs

Patients with a BMI >40 have decreased life expectancy by 8 yrs

BMI ≥35 is equivalent to 70% risk of developing DM2

10% of US healthcare costs are spent treating complications of obesity
Obesity: a Ticking Time Bomb
Health Consequences of Obesity

People who are obese are...
25% more likely to be DEPRESSED

30% of people suffering DEMENTIA are obese

Obese children are 200% more likely to develop MULTIPLE SCLEROSIS

33% more likely to develop ASTHMA

Over 50% of adults living with DIABETES are obese

Nearly 10% of all CANCER is caused by obesity

People who are obese are...
104% more likely to have HEART FAILURE

150% more likely to have HIGH BLOOD PRESSURE

Sources: Centers for Disease Control and Prevention | Harvard Medical School | Heart Rhythm Society | The Sleep Foundation | National Health and Nutrition Examination Survey
Obesity is the Primary Risk Factor for Type 2 Diabetes

Age-adjusted relative risk of type 2 diabetes

Men

- <23: 1.0
- 25: 2.2
- 31: 12
- ≥35: 42

Women

- <22: 1.0
- 25: 8.1
- 31: 40
- ≥35: 93

Benefits of Weight Loss

Weight loss of 5-10% of initial body weight can:

- improve glucose control
- reduce blood pressure
- improve cholesterol levels

Each average 1-kg (2.2-pound) weight loss is associated with a 3-4 month survival increase

<table>
<thead>
<tr>
<th>Health benefits of a 10kg weight loss for those who are obese</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
</tr>
<tr>
<td>20-25% fall in total mortality</td>
</tr>
<tr>
<td>30-40% fall in diabetes deaths</td>
</tr>
<tr>
<td>40-50% fall in obesity related cancer deaths</td>
</tr>
<tr>
<td><strong>Blood pressure</strong></td>
</tr>
<tr>
<td>Fall of 10 mmHg systolic pressure</td>
</tr>
<tr>
<td>Fall of 20 mmHg diastolic pressure</td>
</tr>
<tr>
<td><strong>Lipids</strong></td>
</tr>
<tr>
<td>Fall by 10% in total cholesterol</td>
</tr>
<tr>
<td>Fall by 15% in “bad” cholesterol</td>
</tr>
<tr>
<td>Fall by 30% in triglycerides</td>
</tr>
<tr>
<td>Increase by 8% in “good” cholesterol</td>
</tr>
<tr>
<td><strong>Angina</strong></td>
</tr>
<tr>
<td>Reduced symptoms by 91%</td>
</tr>
<tr>
<td>33% increase in exercise tolerance</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
</tr>
<tr>
<td>Fall of 30-50% in fasting blood glucose</td>
</tr>
<tr>
<td>Reduces risk of developing diabetes by more than 50%</td>
</tr>
</tbody>
</table>
Use healthy oils (like olive and canola oil) for cooking, on salad, and at the table. Limit butter. Avoid trans fat.

The more veggies – and the greater the variety – the better. Potatoes and French fries don’t count.

Eat plenty of fruits of all colors.

Drink water, tea, or coffee (with little or no sugar). Limit milk/dairy (1-2 servings/day) and juice (1 small glass/day). Avoid sugary drinks.

Eat a variety of whole grains (like whole-wheat bread, whole-grain pasta, and brown rice). Limit refined grains (like white rice and white bread).

Choose fish, poultry, beans, and nuts; limit red meat and cheese; avoid bacon, cold cuts, and other processed meats.

STAY ACTIVE!

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Harvard T.H. Chan School of Public Health
The Nutrition Source
www.hsph.harvard.edu/nutritionsource

Harvard Medical School
Harvard Health Publications
www.health.harvard.edu
Daily exercise and weight control

Whole grain foods (at most meals)

Plant oils (olive, canola, soy, corn, sunflower, peanut, and other vegetable oils)

Fruits, 2–3 times/day

Vegetables (in abundance)

Nuts, legumes, 1–3 times/day

Fish, poultry, eggs, 0–2 times/day

Dairy or calcium supplement, 1–2 times/day

Multiple vitamins for most

Alcohol in moderation (if appropriate)

Use sparingly

White rice, white bread, white pasta; potatoes, soda, and sweets

Red meat, butter

Image
EAT THIS, NOT THAT

Small changes in what you eat can help you control your blood sugar, lose weight, and feel better.

Below is a list of foods many of us eat. The “Eat this…” foods have less sugar, salt, bad fats, or cholesterol. Choosing more “Eat this…” foods when you shop and when you eat can help you control your diabetes.

Instead of this
- Eggs
- White bread
- Whole milk, 2% milk
- Butter, margarine, lard
- Cheese
- Flour (or fried) tortillas
- Refried beans
- Canned fruit in heavy/light syrup
- Canned vegetables
- Cookies, cake, chips, ice cream
- Fast food (hamburgers, fries)
- Soda and other drinks with sugar
- Processed meats (hot dogs, Spam, bologna, salami)

Eat this
- Egg whites
- Wheat, whole-grain or multigrain bread
- Fat-free milk, 1% milk
- Vegetable, canola, or olive oil; spray oils
- Low-fat or skim cheese
- Corn or whole-wheat tortillas
- Whole beans, natural beans
- Fresh, frozen, or canned fruit in its own juice
- Fresh or frozen vegetables with no sauce
- Fresh fruit, graham or animal crackers, angel food or sponge cake with fruit, low-fat yogurt
- Salads at fast-food restaurants are often healthy, good-tasting choices
- Water, diet soda, seltzer
- Low-salt turkey, grilled chicken, low-fat (lean) meat, homemade tuna salad

Read food labels when you shop. Look for foods low in sugar, salt, saturated fat (the “bad fat”), and cholesterol. And, always remember to watch your portion sizes when you eat.

Eating is a habit, and changing habits takes time. Start by changing one or two foods. Then change another food every week or so. Eating new foods and trying new ways of cooking can be fun. Enjoy!
THE ACTIVITY PYRAMID

EACH WEEK, TRY TO INCREASE YOUR PHYSICAL ACTIVITY USING THIS GUIDE. HERE'S HOW TO START...

IF YOU ARE INACTIVE
(Rarely do activity)
Increase daily activities at the base of the Activity Pyramid by
- taking the stairs instead of the elevator
- hiding the TV remote control
- making extra trips around the house or yard
- stretching while standing in line
- walking whenever you can

LEISURE ACTIVITIES
GOLF
BOWLING
SOFTBALL
YARDWORK

2-3 TIMES A WEEK
FLEXIBILITY AND STRENGTH
STRETCHING/YOGA
PUSH-UPS/CURL-UPS
WEIGHT LIFTING

IF YOU ARE SPORADIC
(Active some of the time, but not regularly)
Become consistent with activity by increasing activity in the middle of the pyramid by
- finding activities you enjoy
- planning activities in your day
- setting realistic goals

AEROBIC EXERCISE
(BRISK WALKING)
(CROSS-COUNTRY SKIING)
(BICYCLING)
(SWIMMING)

3-5 TIMES A WEEK
RECREATIONAL
(SOCCER)
(HIKING)
(BASKETBALL)
(TENNIS)
(Martial Arts)
DANCING

IF YOU ARE CONSISTENT
(Active most of the time, or at least four days each week)
Choose activities from the whole pyramid by
- changing your routine if you start to get bored
- exploring new activities

ABOVE ALL...
HAVE FUN AND
GOOD LUCK!

WALK THE DOG
TAKE LONGER ROUTES
TAKE THE STAIRS INSTEAD OF THE ELEVATOR

EVERYDAY
(WALK TO THE STORE OR THE MAILBOX)
(WORK IN YOUR GARDEN)
(PARK YOUR CAR FARThER AWAY)
(MAKE EXTRA STEPS IN YOUR DAY)

BE CREATIVE IN FINDING A VARIETY OF WAYS TO STAY ACTIVE

CUT DOWN ON
WATCHING TV
COMPUTER GAMES
SITTING FOR MORE THAN 30 MINUTES AT A TIME

(AS MUCH AS POSSIBLE)
Indications to Treat Obesity

Indications for weight loss medication:

BMI $\geq 30$ or

BMI $\geq 27$ with obesity related comorbidities (DM, HTN, HLD, OSA, NASH, GERD, Asthma, urinary incontinence, debilitating arthritis, pseudotumor cerebrii)

Indications for bariatric surgery:

BMI $\geq 40$ with no comorbidities or

BMI $35-39.9$ with one or more obesity related comorbidity (DM, HTN, HLD, OSA, NASH, GERD, Asthma, urinary incontinence, debilitating arthritis, pseudotumor cerebrii)
FDA Approved Medications for Obesity

<table>
<thead>
<tr>
<th>Agent</th>
<th>Mechanism of Action</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diethylpropion</td>
<td>Norepinephrine-releasing agent</td>
<td>Approved for short-term use (3 months)</td>
</tr>
<tr>
<td>Liraglutide (Saxenda)</td>
<td>GLP-1 receptor agonant</td>
<td></td>
</tr>
<tr>
<td>Lorcanser (Belviq)</td>
<td>5HT2c receptor agonant</td>
<td>Recommended for patients with cardiovascular disease</td>
</tr>
<tr>
<td>Naltrexone/bupropion (Contrave)</td>
<td>Opioid antagonist/dopamine and norepinephrine reuptake inhibitor</td>
<td></td>
</tr>
<tr>
<td>Orlistat, prescription (120 mg, Xenical) and over-the-counter (60 mg, Alli)</td>
<td>Pancreatic and gastric lipase inhibitor</td>
<td>Recommended for patients with cardiovascular disease</td>
</tr>
<tr>
<td>Phentermine</td>
<td>Norepinephrine-releasing agent</td>
<td>Approved for short-term use (3 months); Not recommended in patients with uncontrolled hypertension or heart disease</td>
</tr>
<tr>
<td>Phentermine/Topiramate (Qsymia)</td>
<td>Norepinephrine-releasing agent/GABA receptor modulation agent</td>
<td></td>
</tr>
</tbody>
</table>

GABA, γ-aminobutyric acid; GLP-1, glucagon-like peptide-1
Diethylpropion

- FDA approved for short term use
  - usually considered <12 weeks

- **Action:** Reduces appetite by increasing activation of adrenergic and dopaminergic receptors

- **Benefits:** 9 small studies ranging from 6-52 weeks found that pts using diethylpropion 75mg/day had a mean additional weight loss relative to placebo of 3kg (6.2lbs) with a mean total weight loss of 6.5kg (14.3lbs)

- **Side Effects:** increase in HR, less decrease in BP as would be expected by the amount of weight loss, no long term data on cardiovascular effects

- **Contraindications:** Arrhythmia, Severe Hypertension, Hyperthyroidism

- **Dosing:** 25mg orally three times a day before meals
Effects of Dopamine on Satiety

- Dopamine is released in response to a food reward

- Over time, the brain will become accustomed to the stimuli of upcoming food, for example the smell of food, and expect that there will be an upcoming dopamine release

- Exposure to food cues elicits dopamine increases that are associated with the desire to eat the food, even if the person is full

- Decreases in dopamine receptors have been linked to compulsive food intake in obese rodents

- It is thought that obese individuals have increased sensitivity of the reward circuitry to conditioned stimuli (viewing high-calorie food) that predict reward, but a decreased sensitivity to the rewarding effects of actual food consumption in dopaminergic pathways

- There is a mismatch between the expected reward and a delivery that does not fulfill this expectation, this will promote compulsive eating as an attempt to achieve the expected level of reward
Change from baseline for body weight over 1 year. After 6 months, all participants received diethylpropion (open-label phase).

Number of patients achieving weight loss of 5 and 10% according to the group assignment at months 6 and 12. Placebo switched to diethylpropion on open-label phase (months 7–12).
Phentermine

- **FDA approval for short term use**
  - however it is frequently prescribed off-label for longer periods

- **Action:** reduce appetite by increasing activation of adrenergic and dopaminergic receptors

- **Benefits:** pts using 15-30mg/day had a mean additional weight loss relative to placebo of 3.6kg, with mean total weight loss of 6.3kg (13.86 lbs)

- **Side Effects:** although it has a long hx of use there are few controlled trials of phentermine monotherapy for 6 months or more, transient symptoms of CNS stimulation such as insomnia, irritability, anxiety, elevations in pulse

- **Contraindications:** uncontrolled hypertension, breastfeeding, hyperthyroidism, agitation

- **Dosing:**
  - 15mg po q AM to 37.5mg po q AM
  - this is the most widely Rx obesity medication in the US (estimated 6.2 million users in US between 2008-2011)
Benefits of Phentermine on Weight Loss

Topiramate and Phentermine (ITT)

Phentermine/Topiramate (Qsymia)

- **Action:**
  - reduce appetite by increasing activation of adrenergic and dopaminergic receptors
  - prolongs satiety
  - makes soda and beer taste flat by decreasing CO2 so pts will drink less soda and beer

- **Benefit:**
  - weight loss of 10-15%
  - decreases risk of Diabetes by 80%
  - approved for long term use

- **Side effects:** constipation, insomnia, anxiety, no change in BP, cleft palate in fetus, parasthesias, Small increase in resting heart rate occurs especially at higher doses, with increases of more than 10bpm, concern for long term CVD events

- **Contraindications:** patient with MI, CVA or increased basal HR, pregnancy (must do a pregnancy test in the office and ensure patient is on birth control method), may increase eye pressure so might not want to use it in pts with glaucoma

- **Dosing:**
  - 3.75mg phentermine/23mg topiramate (starting dose)
  - 7.5mg phentermine/46mg topiramate (recommended dose)
  - 11.25mg phentermine/69mg topiramate (titration dose)
  - 15mg phentermine/92mg topiramate (top dose)
Weight Loss

Benefits of Phentermine/Topiramate
Naltrexone/Bupropion (Contrave)

- **Actions:**
  - Naltrexone is an opioid antagonist
  - Bupropion acts as a reuptake inhibitor of dopamine and norepinephrine
  - together they help to suppresses appetite, cravings, and emotional eating, increased sensation of fullness

- **Benefits:**
  - Weight loss of 5-8%
  - no increase in CV events
  - will decrease waist circumference
  - will decrease Triglycerides, will increase HDL
  - will decrease blood sugars

- **Side effects:** Nausea, vomiting, headache, constipation, dizziness, will increase HR, will increase Blood pressure by 1-2mm Mg more in first 3 months

- **Contraindications:** pregnancy, contraindicated in uncontrolled HTN, lowers seizure threshold so should not be used in history of seizures or alcoholism, should not be used on pts that need opioids for pain

- **Dosing:** 1 tablet (90mg/8mg) initially week 1; increase by 1 tablet/day each subsequent week until daily maintenance dose of 2 tablets twice daily (360 mg bupropion/32 mg naltrexone) is achieved at the start of week 4, increase dose slowly to prevent nausea
# Weight Loss Benefits of Contrave

![Graph showing weight change over weeks for different treatment groups.](image)

## Number of participants by visit (observed)

| Treatment                        | Weeks 0 | Weeks 4 | Weeks 8 | Weeks 12 | Weeks 16 | Weeks 24 | Weeks 28 | Weeks 32 | Weeks 36 | Weeks 40 | Weeks 44 | Weeks 48 | Weeks 52 | Weeks 56 |
|----------------------------------|---------|---------|---------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| Placebo                          | 507     | 463     | 420     | 394      | 365      | 353      | 327      | 318      | 308      | 302      | 296      | 291      | 289      | 277      |
| Naltrexone 16 mg plus bupropion  | 457     | 410     | 373     | 351      | 346      | 341      | 311      | 311      | 302      | 297      | 300      | 284      | 283      | 273      |
| Naltrexone 32 mg plus bupropion  | 467     | 411     | 391     | 372      | 365      | 361      | 343      | 327      | 321      | 316      | 311      | 305      | 298      | 284      |
Lorcaserin (Belviq)

- approved by FDA in 2012, approved for long term use

**Action:** selective serotonin 2C receptor agonist, increases satiety, it tells liver to decrease glucose production, appetite suppressant

**Benefit:**
- Weight loss of 3-5% in 3 months
- safest drug to use in pregnancy
- safest to use in CVD pts
- will decrease cholesterol, decreases LDL, decreases Triglycerides,
- decreases Heart rate
- decreases waist circumference
- very good to use in pts with fatty liver disease,
- fasting blood sugar will decrease by 30mg/dL, decreases HgA1C by 1%,
- no evidence for valvulopathy

**Side Effects:** mild headaches, dizziness, nausea

**Contraindications:** may need to decrease insulin or sulfonylureas by ½ because of risk of hypoglycemia, can increase serotonin and SSRI levels, should not use on pts that use serotonin related drugs, example: Citalopram (Celexa), Escitalopram (Lexapro), Fluoxetine (Prozac), Paroxetine (Paxil, Pexeva), Sertraline (Zoloft)

**Dosing:** 10mg bid
Serotonin Effects on Satiety

Serotonin is involved in sensing satiation during meal and in post-meal satiety.

Serotonin receptors inhibit neuropeptide Y (NPY) which is a potent stimulator of hunger and food intake.
Benefits of Weight Loss with Lorcaserin

A Weight Loss at 1 Yr

- Lorcaserin (N=1538)
- Placebo (N=1499)

\( P < 0.001 \)

<table>
<thead>
<tr>
<th>Patients (%)</th>
<th>( \geq 5% ) Weight Loss</th>
<th>( \geq 10% ) Weight Loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorcaserin</td>
<td>50</td>
<td>20</td>
</tr>
<tr>
<td>Placebo</td>
<td>30</td>
<td>10</td>
</tr>
</tbody>
</table>

B Body Weight during Yr 1

- Lorcaserin (N=1538)
- Placebo (N=1499)

Study Week

C Body Weight during Yr 1 and 2

- Lorcaserin in yr 1 (N=684)
- Placebo in yr 1, placebo in yr 2 (N=275)
- Lorcaserin in yr 1 and 2 (N=564)
Liraglutide (Saxenda)

- FDA approved Dec 2014

- **Action**: GLP-1 agonist, suppresses appetite, delays gastric emptying

- **Benefits**:
  - Weight loss of 7-9% from initial weight
  - Additional weight loss over placebo of 3.5-5.8kg (7.7-12.2 lbs) over 6-12 months
  - After 2 yrs, 50% of all prediabetics using this medication normalize their prediabetes
  - Approved for long term use

- **Side effects**: nausea, vomiting, constipation, diarrhea, concern for pancreatitis and pancreatic cancer

- **Contraindications**: pregnancy or medullary thyroid cancer or history of pancreatitis

- **Dosing**: increase dose weekly to goal of 3mg/day SC
GLP-1 Actions

- Decrease appetite
- Decrease gastric emptying so you feel full longer
- Decrease liver glucose production
- Increase Insulin secretion
- Increase insulin sensitivity
Weight Loss Benefits of Liraglutide
Orlistat (Xenical or Alli)

- FDA approved for use in adults and adolescents age 12-16 y.o. and for indefinite treatment of obesity

- **Action:** Gastrointestinal lipase inhibitor which when taken three times a day during or up to 1 hr after meals, leads to the excretion of approximately 30% of ingested fat

- **Benefits:**
  - weight loss of 3-4%
  - decreased risk of developing diabetes from 9% in placebo to 6% in Orlistat treated patients
  - Decrease in total cholesterol
  - Decrease in LDL cholesterol
  - Decrease in fasting glucose
  - Decrease in systolic and diastolic blood pressures after 1 yr of tx

- **Side effects:** decrease in fat soluble vitamins (Vitamins A, D, E, and K), gas, diarrhea, abdominal pain, stool incontinence

- **Contraindications:** Pregnancy, Chronic malabsorption syndromes, cholestasis

- **Dosing:** Xenical 120mg tid with meals, Alli 60mg po tid
Weight Loss Benefits of Orlistat

Graph showing changes in weight, insulin levels, low-density lipoprotein cholesterol, and total cholesterol over time with Orlistat and Placebo treatments.
## Review of FDA approved Medications for Obesity

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Status</th>
<th>Mechanism</th>
<th>Dosing</th>
<th>Response evaluation</th>
<th>Warnings</th>
<th>Contraindications</th>
<th>Side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orlistat</td>
<td>FDA &amp; EMA approved</td>
<td>pancreatic, gastric lipase inhibitor</td>
<td>120 mg tid (60 mg tid (OTC))</td>
<td>2.9-3.4% 1 year</td>
<td>hepatitis, liver failure (rare), concomitant multivitamin advised</td>
<td>pregnancy, breast feeding, chronic malabsorption syndrome, cholestasis</td>
<td>decreased absorption of fat soluble vitamins, steatorrhea, faecal urgency</td>
</tr>
<tr>
<td>Lorcanin</td>
<td>FDA approved</td>
<td>5HT2c R agonist</td>
<td>10 bid</td>
<td>3.6% 1 year stop if &lt;5% weight loss at 12 weeks</td>
<td>serotonin syndrome, cognitive impairment, depression, valvulopathy hypoglycaemia, priapism</td>
<td>pregnancy, breast feeding, use with caution: MAOIs, SSRIs, SNRIs</td>
<td>headache, nausea dry mouth, dizziness fatigue, constipation</td>
</tr>
<tr>
<td>Phentermine/ topiramate</td>
<td>FDA approved</td>
<td>NE release (P) GABA modulation (T)</td>
<td>starting dose: 3.75/23 qd recommended dose: 7.5/46 qd *high dose: 15/92 qd</td>
<td>6.6% (recommended dose) 1 year 8.6% (high dose) 1 year stop if &lt;5% weight loss at 12 weeks</td>
<td>fetal toxicity, acute myopia, cognitive dysfunction, metabolic acidosis, hypoglycaemia</td>
<td>pregnancy, breast feeding, glaucoma, hyperthyroidism, use with caution: MAOIs</td>
<td>insomnia, dry mouth constipation, paresthesia, dizziness, dysgeusia</td>
</tr>
<tr>
<td>Bupropione/ naltrexone</td>
<td>FDA &amp; EMA approved</td>
<td>DA/NE reuptake inhibitor (B) opioid antagonist (N)</td>
<td>8/90 mg tb 2 tb bid</td>
<td>4.8% 1 year stop if &lt;5% weight loss at 12 weeks</td>
<td>fetal toxicity, increased seizure risk, glaucoma, hepatotoxicity</td>
<td>uncontrolled hypertension, seizure, anorexia nervosa / bulimia, drug or alcohol withdrawal, use with caution: MAO inhibitors</td>
<td>nausea, constipation, headache, vomiting, dizziness</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>FDA &amp; EMA approved</td>
<td>GLP-1 agonist</td>
<td>3 mg sc</td>
<td>5.8 kg 1 year stop if &lt;4% weight loss at 14 wks</td>
<td>acute pancreatitis, acute gall bladder disease</td>
<td>medullary thyroid cancer history, MEN type 2 history</td>
<td>nausea, vomiting, pancreatitis</td>
</tr>
</tbody>
</table>

FDA = Food & Drug Administration; EMA= European Medicinal Agency; OTC = over the counter; 5HT2c-R = 5 hydroxytryptamine 2c receptor; MAOI = monoamino oxidase inhibitor; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin norepinephrine reuptake inhibitor; NE = norepinephrine; GABA = gamma amino butyric acid; DA = dopamine; GLP-1 = glucagon-like peptide-1; MEN = multiple endocrine neoplasia.

*Careful observation.
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