# Pharmacotherapy

FDA Approved Medications for Weight Loss

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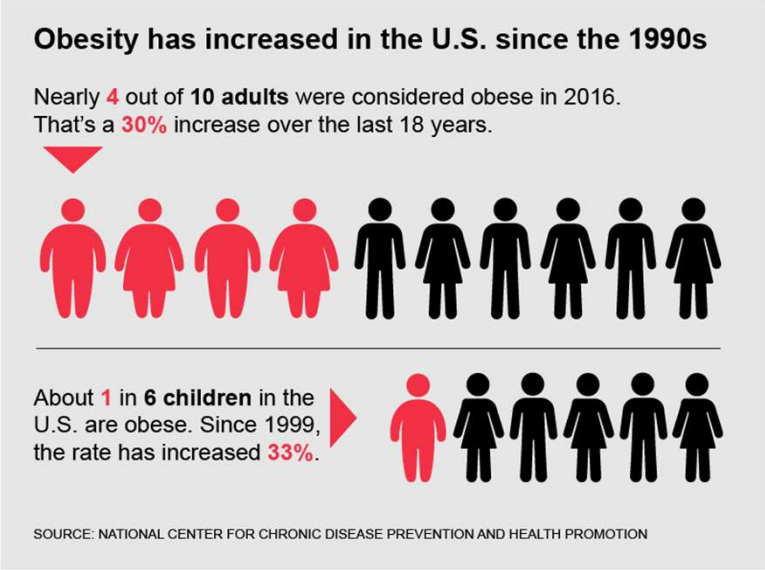
# Disclosures

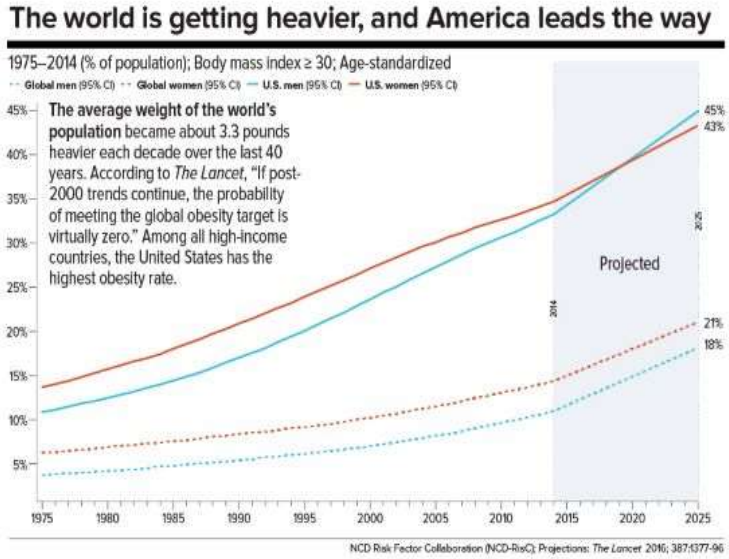
- OMA Board of Trustees
- No Financial Disclosures

# Objectives

- Recognize and discuss indications for medication for weight loss.
- Explain medications for weight loss.
- Discuss common side-effects and be comfortable using FDA approved medications for weight loss.

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.



# Anti-Obesity Medications

- Adjunct to nutritional, physical activity and behavioral therapies.
- 5-10 percent weight loss improves metabolic and fat mass disease.

Objectives:

- Treat disease.
- Facilitate management of eating behavior.
- Prevent weight gain/regain.
- Improve the health, quality of life, and body weight of the patient with overweight or obesity.

# Food and Drug Administration (FDA) Principles

FDA-approved Anti-obesity Medication 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)*
- Anti-obesity medications are contraindicated in patients hypersensitive to the drugs

Other Principles

- Anti-obesity medications promote variable weight loss over variable duration in patients with overweight or obesity.
- Some patients having an 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.
- If no clinical improvement (e.g., at least 4 - 5% loss of baseline body weight) after 12-16 weeks with one anti-obesity medication, then consider alternative anti-obesity medication or increasing anti-obesity medication dose (if applicable).

*While body mass index (BMI) is the only measure listed in the prescribing information for anti-obesity medications, BMI has limitations. Especially in muscular individuals or those with sarcopenia, overweight and obesity are more accurately assessed by other measures.

# Regulations

- Always check with your local and state medical/pharmacy boards and malpractice insurance before prescribing anti-obesity medications.
- Local and state laws and regulations may vary.

# FDA Approved AOMS for Long Term Use

**Orlistat**
Trade Names:
Xenical (1999)
Alli® (2007)

**Phentermine/ Topiramate ER**
Trade Name:
Qsymia® (2012)

**Naltrexone/ Bupropion ER**
Trade Name: Contrave®(2014)

**Liraglutide**
Trade Name:
Saxenda® (2014)

**Semaglutide**
Trade Name:
Wegovy® (2021)

**Setmelanotide**
Trade Name: Imcivree™(2020)

**Table. FDA-Approved Medications for Chronic Weight Management**

| | FDA Approval Year | Pharmacologic Class | Usual Maintenance Dose | Frequency | Route | Mean Reduction in Body Weight* | Monthly Cost (AWP)† |
|---|---|---|---|---|---|---|---|
| Semaglutide (Wegovy) | 2021 | GLP-1 agonist | 2.4 mg | Weekly | SQ | 9.6 to 16%‡ | $1,619 |
| Liraglutide (Saxenda) | 2014 | GLP-1 agonist | 3 mg | Daily | SQ | 4.9 to 7.4%‡ | $1,619 |
| Naltrexone ER/ Bupropion ER (Contrave) | 2014 | Opioid antagonist/ antidepressant | 16 mg/180 mg (equivalent to 2 tablets) | Twice daily | PO | 3.7 to 8.1%‡ | $364 |
| Phentermine/ Topiramate ER (Qsymia) | 2012 | Sympathomimetic/ anticonvulsant | 15 mg/92 mg | Daily | PO | 9.8 to 10.9%§ | $239 |
| Orlistat (Alli, OTC; Xenical, Rx) | 2007, Alli; 1999, Xenical | Lipase inhibitor | 60 mg, Alli; 120 mg, Xenical | Three times daily | PO | 4.6 to 10.2%¶, Xenical | $41, Alli; $823, Xenical |

*As reported in clinical trials when used at doses provided in the table along with lifestyle modifications
†Average Wholesale Price (AWP) according to Red Book (accessed via IBM Micromedex on June 22, 2021)
‡Results from 3 studies involving each of the medications
§Results from 2 studies involving this medication
¶According to the 2016 American Association of Clinical Endocrinologists and the American College of Endocrinology guideline



# Reference?

# ORLISTAT

| Indications | Chronic Obesity Management |
|---|---|
| Dosage | 60mg (Alli OTC) – 120mg (Xenical Rx) capsule TID with each meal |
| MOA | Pancreatic & Gastric Lipase Inhibitor, prevents absorption of ~30% of ingested fat |
| Contraindications | Pregnancy, Chronic malabsorption syndrome, cholestasis, known hypersensitivity to Orlistat |
| ADRs | Diarrhea, Oily stools, Fecal incontinence, Rare hepatotoxicity, Fat soluble vitamin deficiency, increase urinary oxalate stones |
| Weight Loss | 3.9%, 2 year 2.3% |
| Clinically significant wt loss | >5% wt loss:21%<br>>10% wt loss : 12% |
| Pharmacokinetics | Metabolism likely occurs within the GI wall; systematic exposure to Orlistat is minimal |

# PHENTERMINE/TOPIRAMATE ER

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Dosage | Start AM dosing 3.75/23mg X 14 days<br>Increase to 7.5/46mg<br>If weight loss <3% after 12 weeks increase dose 11.25/69mg x 14 days; then increase to 15/92mg (full strength)<br>D/C med if <5% weight loss at 12 weeks @ max dose. | DEA Schedule IV drug<br>Important: need to titrate QOD dosing for at least 7 days if discontinuing the med from 15/92 mg dose to reduce seizure risk |
| Mechanism of action (MOA) | Phentermine is a sympathomimetic amine and its effect on obesity management is likely mediated by release of catecholamines (NE) in the hypothalamus resulting in decreased appetite and food intake. | Topiramate exact MOA for chronic weight management unknown; effects may be due to appetite and increased satiety induced by augmenting GABA activity or inhibiting carbonic anhydrase. |
| Pharmacokinetics | Phentermine is metabolized by the liver, with most excreted by the kidney<br>Topiramate is excreted mainly by the kidney | Caution with decreased kidney function |

# PHENTERMINE/TOPIRAMATE ER

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Clinical trials weight loss (WL) | 2 studies, over 3700 patients total | -10.9% WL 15/92<br>- 5.1% WL 7.5/46<br>- 1.6% WL placebo |
| Responder rates | 5% WL: 67% at full dose , 17% placebo<br>10% WL: 47% at full dose, 7% placebo | |
| Contraindications | Symptomatic coronary artery disease, active mania, uncontrolled hypertension, closed angle glaucoma, pregnancy, calcium oxalate nephrolithiasis, concomitant MAOI use within 14 days | Monitoring: monitor for pregnancy and continued OCP in child-bearing women |
| Adverse Drug Reactions | Common: paresthesias, dizziness, dysgeusia, insomnia, constipation, dry mouth, disturbance in attention<br>Serious: metabolic acidosis, nephrolithiasis, acute angle closure , glaucoma, depression and suicidal ideation | REMS: fetal toxicity (oral cleft lip/palate); check urine pregnancy monthly (can be done by patient at home) or document 2 forms contraception |

# NALTREXONE/BUPROPION HCL ER

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Dosage | Titration 8mg naltrexone/90mg bupropion over the course 4 weeks: Week 1: 1 tablet in AM<br>Week 2: 1 tablet in AM and PM<br>Week 3: 2 tablets in AM and 1 tablet in PM<br>Week 4: 2 tablets in AM and 2 tablets in PM | Each tablet contains 8/90mg ER of naltrexone and bupropion. |
| MOA | Naltrexone: opioid antagonist that may work in hypothalamus and mesolimbic/dopamine circuit to decrease appetite and reward; exact MOA not fully understood | Bupropion: weak inhibitor of neuronal reuptake of dopamine and NE that may work in hypothalamus and mesolimbic/dopamine circuit to decrease appetite and reward; exact MOA not fully understood |
| Pharmacokinetics | Bupropion is extensively metabolized into biologically active metabolites; 87% of bupropion and metabolites excreted by kidneys Naltrexone excreted primarily via kidneys | Bupropion and its metabolites inhibit CYP2D6 inhibitor; caution for drug interactions |

# NALTREXONE/BUPROPION HCL ER

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Clinical trials weight loss | 4 RCT double blind studies over 4500 patients | COR-1 -5.4% treatment vs -1.3% placebo<br>COR-BMOD -8.1% treatment vs -4.9% placebo |
| Clinically significant weight loss rates | 5% WL: 42% treatment<br>17% placebo (COR-1)<br>10% WL: 21% treatment<br>7% placebo<br>COR-BMOD<br>5% WL: 57% treatment<br>43% placebo<br>10% WL: 35% treatment<br>21% placebo | Monitoring: Label says if has not had >5 % weight loss at 12 weeks to discontinue therapy |

# NALTREXONE/BUPROPION HCL ER

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Contraindications | Uncontrolled HTN, Seizure D/O, anorexia nervosa, bulimia, OR undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates or anti-epileptics; chronic opioid use, concomitant MAOI usage within 14 days | BOXED WARNING: increased suicidal ideation and/or behavior in children, adolescents, or young adults seen with bupropion containing products, monitor for changes; neuropsychological events seen with bupropion and its usage in smoking cessation |
| Adverse Drug Reactions | Common: Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea<br>Serious: worsening depression, suicidal ideation, hepatotoxicity, seizures | Caution: avoid concomitant opioid use and with high fat foods |

# GLP-1 RECEPTOR AGONISTS (LIRAGLUTIDE & SEMAGLUTIDE)

| **Indications** | **Chronic Obesity Management** | **BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity** |
|---|---|---|
| Dosage | Liraglutide 3.0 mg sc daily and Semaglutide 2.4 mg sc weekly are approved only for the treatment of obesity | |
| Mechanism of action (MOA): | Liraglutide and Semaglutide are **GLP-1 receptor agonists** administered subcutaneously. Administration **activates specific areas in the hypothalamus reducing food intake, increasing satiety, and decreasing caloric intake** as well as improving glucose | Liraglutide has 97 % and Semaglutide 94 % homology to endogenous GLP-1 |
| Contraindications: | Personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome type 2; Hypersensitivity to liraglutide or any product components; Pregnancy | BLACK BOX: counsel patients that liraglutide causes C-cell tumors at clinically relevant exposures in both genders of rats and mice; unknown whether liraglutide causes thyroid Ccell tumors, including medullary thyroid carcinoma (MTC), in humans |
| Adverse Drug Reactions | Nausea, hypoglycemia, diarrhea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue, dizziness, abdominal pain, and increased lipase; if nausea, hydrate, consider pancreatitis, encourage low fat and small meals | PRECAUTIONS: Acute pancreatitis, acute gall bladder disease, serious hypoglycemia when used with insulin or insulin secretagogues, increased heart rate, renal impairment, suicidal behavior Monitor: for adequate hydration and if inadequate for AKI |

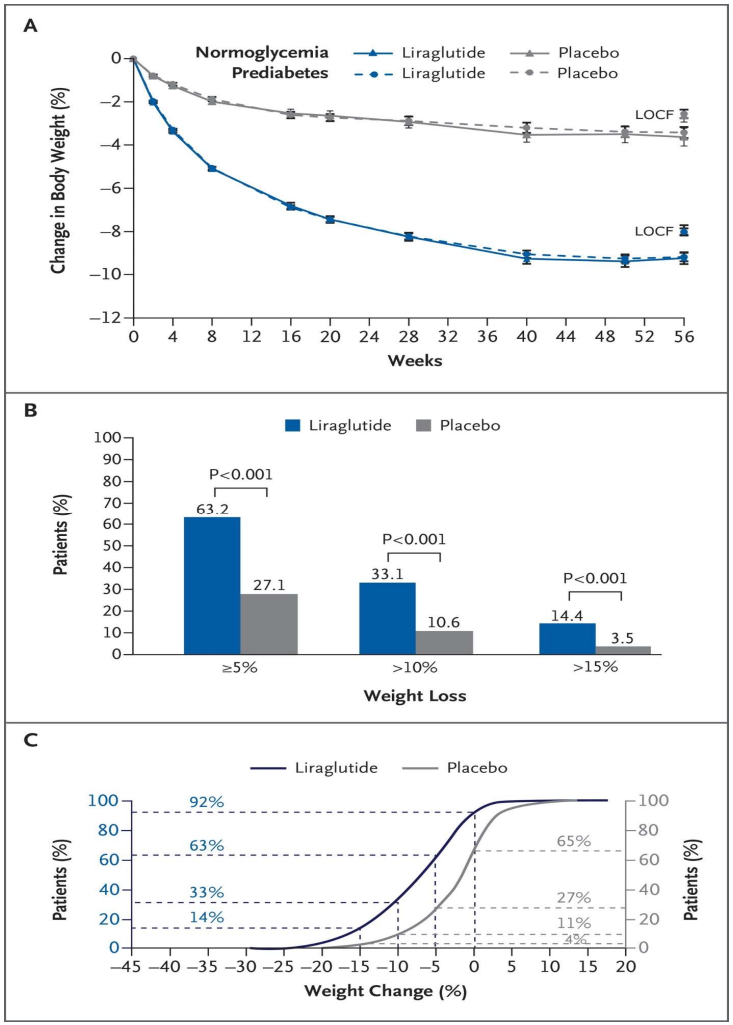
# LIRAGLUTIDE

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Dosage | Titration over 5 weeks once daily subcutaneous injection: Week 1: 0.6mg SC x 7 days Week 2: 1.2mg SC x 7 days Week 3: 1.8mg SC x 7 days Week 4: 2.4mg SC x 7 days Week 5: 3.0mg SC ongoing (maintenance dose) | Use daily Can change injection site and timing without dose adjustment If <4% weight loss after 16 weeks consider discontinuing medication |
| Mechanism of action (MOA): | Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist with 97% homology to endogenous GLP-1; peripheral administration resulted in activation of specific areas in hypothalamus reducing food intake, increased satiety, and decreased caloric intake as well as improving glucose metabolism | |
| Pharmacokinetics | Liraglutide is endogenously metabolized similarly to other large proteins without a specific organ as a major route of elimination. Intact liraglutide not excreted; Only 5-6 % of liraglutide metabolites found in urine or feces | Approx. 55% bioavailable regardless of injection site (upper arm, abdomen, or thigh) |

# LIRAGLUTIDE

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Clinical trials weight loss (WL): | 3 studies over 4700 patients 56 weeks double blind RCT<br>3-year study patients with prediabetes 160 weeks (Although not an indication for use, benefits seen for PCOS and progression of pre-diabetes to diabetes) Pani 2020 | WL: -9.2% treatment v. -3.5% placebo<br>WL: -6.1% treatment v. 1.9% placebo |
| Clinically significant weight loss rates | 5% WL: 62% at full dose<br>34% placebo<br><br>10% WL: 34% at full dose<br>15% placebo | |

# LIRAGLUTIDE




X. Pi-Sunyer and Others N Engl J Med 2015; 373:11-22

# SEMAGLUTIDE

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Dosage | Titrate every 4 weeks for 5 months; once weekly subcutaneous injection:<br>Week 1-4: 0.25mg SC weekly<br>Week 5-8: 0.5mg SC weekly<br>Week 9-12: 1.0mg SC weekly<br>Week 13-16: 1.7 mg SC weekly<br>Week 17 and thereafter: 2.4 mg weekly (maintenance dose) | Administer once weekly on the same day with or without meals. If the 2.4 mg dose is not tolerated, it may be reduced to 1.7 mg per week for ≤ 4 weeks. If the 2.4 mg dose is still not tolerated, Semaglutide should be discontinued |
| Pharmacokinetics | The primary route of elimination for Semaglutide is metabolism following proteolytic cleavage of the peptide backbone and sequential betaoxidation of the fatty acid sidechain. Semaglutide is 98 % bound to albumin, significantly reducing renal clearance protecting it from degradation. Excretion routes are primarily urine and feces with 3 % as intact Semaglutide. | 89% bioavailability regardless of injection site. Peak levels 1-3 days after injection. Half life is one week; detectable levels persist 5-7 weeks following a 2.4 mg dose. |

# SEMAGLUTIDE

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Clinical trials weight loss (WL): | 3 studies 68 weeks double blind RCT patients with obesity/overweight Semaglutide 2.4 mg SC weekly<br>Study 1: 1306 pts with ≥ 1 co-morbidity<br>Study 2: 404 pts with T2DM<br>Study 3: 407 pts: Semaglutide ≥ 1 comorbidity + intensive lifestyle intervention<br>Most effective treatment we have at higher doses | Semaglutide 2.4 mg Placebo<br>WL 14.9% 2.4%<br>WL 9.6% 3.4%<br>WL 16.0% 5.7% |
| Clinically significant weight loss rates (Study 3 with intensive lifestyle intervention) | 5% WL: 84.8% Semaglutide 2.4 mg weekly<br>47.8% Placebo<br><br>10% WL: 73.0% Semaglutide 2.4 mg weekly<br>27.1% Placebo<br><br>15% WL 53.4% Semaglutide 2.4 mg weekly<br>13.2% Placebo | Approved only for obesity treatment, but evidence suggests improvement in studies using Semaglutide 1 mg in fasting and pp glucose in pt w/o diabetes, and beneficial effects on lipids, and improvement in NASH |

RESEARCH SUMMARY

# Once-Weekly Semaglutide in Adults with Overweight or Obesity

Wilding JPH. et al. DOI: 10.1056/NEJMoa2032183

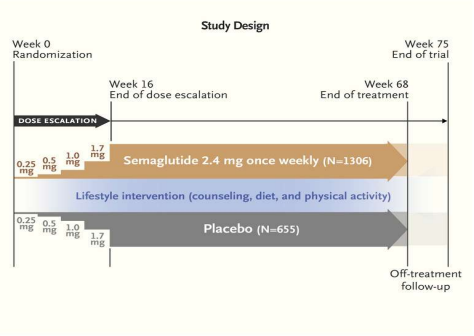
## CLINICAL PROBLEM

Clinical guidelines suggest pharmacologic intervention in addition to diet and exercise to promote weight loss among adults with BMI ≥30 (or ≥27 in those with coexisting conditions). Barriers to medication use include limited efficacy, adverse effects, and cost. Subcutaneous semaglutide, a glucagon-like peptide-1 analogue FDA-approved to treat type 2 diabetes in adults, has been accompanied by weight loss in previous clinical trials.

## CLINICAL TRIAL

A phase 3, double-blind, randomized, controlled trial comparing semaglutide with placebo, plus lifestyle changes, in overweight or obese adults without diabetes.

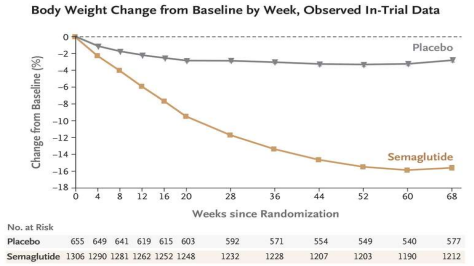
1961 participants were assigned to receive 2.4 mg of subcutaneous semaglutide (with gradual increase to the 2.4 mg dose) or placebo weekly for 68 weeks; both groups received a counseling intervention involving diet and exercise. Coprimary end points were percentage change in body weight and weight reduction ≥5%.




## RESULTS

**Efficacy:**
By week 68, mean weight declined more with semaglutide than with placebo (14.9% vs. 2.4%; estimated difference, –12.4 percentage points; 95% CI, –13.4 to –11.5). In addition, more participants in the semaglutide group than in the placebo group had weight loss of ≥5% (86.4% vs. 31.5%).

**Safety:**
Adverse events, mainly gastrointestinal, were most often mild to moderate but led to treatment discontinuation in 7.0% of the semaglutide group and 3.1% of the placebo group. Serious adverse events, primarily gastrointestinal and hepatobiliary events, were reported more often with semaglutide.




## LIMITATIONS AND REMAINING QUESTIONS

**Limitations:**
- 43.7% of participants had prediabetes and might have responded differentially to the effects of semaglutide on weight gain.

**Further study is required to understand the following:**
- Whether results would be similar in persons who differ from the study participants, who were mainly female, White, and potentially highly motivated to lose weight
- Longer-term outcomes
- The mechanism by which semaglutide affects weight-related measures of health (e.g., body composition and glycated hemoglobin) in patients without diabetes

**Links: Full article | NEJM Quick Take | Editorial**

## CONCLUSIONS

**Adults without diabetes who were overweight or obese had clinically relevant weight loss with weekly injections of semaglutide (2.4 mg) added to lifestyle changes.**



J.P. Wilding and Others N Engl J Med 2021; 384:989-1002

# SETMELANOTIDE

| Indications | Obesity management in adults and children ≥ 6 years with obesity due to genetic defects in POMC, PCSK-1, or LEPR (leptin receptor deficiency) | Genetic testing must confirm either pathogenic, likely pathogenic or of uncertain significance |
|---|---|---|
| Dosage | Adults and children ≥ 12 yo: 2 mg sc once daily X 2 wks; titrate dose up to 3 mg sc daily (if not tolerated may use lower dose)<br>Children 6-11 yo: 1 mg sc daily for 2 wks; titrate to 2 mg sc. If not tolerated may reduce dose to 0.5-1.0 mg qd Monitor for GI side effects in adults and children | 10 mg/ml multi-dose vials |
| Mechanism of action (MOA): | Setmelanotide reestablishes the MC4 receptor pathway in persons with obesity who have deficiencies in POMC, PCSK-1, or LEPR. Activation of MC4 receptors reduces hunger and increases energy expenditure resulting in weight loss in persons with these genetic variants. | |
| Pharmacokinetics | Steady state plasma concentrations are achieved in 2 days. Protein binding is 79.1 % and ½ life is 11 hours. Setmelanotide is broken down into small peptides; 39 % excreted unchanged in the urine. | |

# SETMELANOTIDE

| Indications | Obesity management in adults and children ≥ 6 years with obesity due to genetic defects in POMC, PCSK-1, or LEPR (leptin receptor deficiency) | Genetic testing must confirm either pathogenic, likely pathogenic or of uncertain significance |
|---|---|---|
| Clinical Weight loss trials | 2 one -year studies in adults with BMI ≥ 30 kg/m² and children ≥ 6 years of age and BMI ≥ 95th percentile on growth chart with confirmed POMC or PCSK-1 deficiency (study 1) or LEPR deficiency (Study 2).<br>Study 1 included 10 pts; Study 2 had 11 pts | % change in mean body weight at one year Study 1: 25.6 %Study 2: 12.5 % |
| Clinically significant weight loss rates: | 80 % achieved a 10 % weight loss in study 1 45.5 % achieved 10 % weight loss in Study 2 | |
| Contraindications: | No contraindications. There is no available data for use in pregnancy. Discontinue during pregnancy unless benefits outweigh risks. | |
| Most common ADR: | Clinically significant: Spontaneous penile erection; depression and suicidal ideation; skin pigmentation and darkening of existing nevi. | More common: Injection site pain and pigmentation. GI effects (nausea, diarrhea abdominal pain, vomiting); headache, back pain and fatigue reported ≥ 30 %. |

# ANTI-OBESITY DRUGS (SHORT TERM USE)

## Drugs Approved by the FDA for Treating Obesity

| Generic Name | Trade Names | Approved Use | Year Approved |
|---|---|---|---|
| Orlistat | Xenical | Long-term | 1999 |
| Sibutramine | Reductil/Meridia | Long-term | 1997 |
| Diethylpropion | Tenulate | Short-term | 1973 |
| Phenetermine | Adipex, lonamin | Short-term | 1973 |
| Phedimetrazine | Bontril, Prelu-2 | Short-term | 1961 |
| Benzphetamine | Didrex | Short-term | 1960 |

# PHENTERMINE

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Dosage | 8 mg (Lomaira®), 15 mg or 30 mg capsules hydrochloride salt or resin form, or 37.5 mg scored tablets (Adipex-P®) | Commonly doses are 15-37.5 mg daily; most cost-effective treatment we have |
| Mechanism of action (MOA) | Sympathomimetic amine stimulating hypothalamus to secrete norepinephrine among other CNS effects | |
| Pharmacokinetics | Phentermine is metabolized by the liver, with most excreted by the kidney. Eliminated primarily via urine (62-85%); use with caution when administering phentermine to patients with renal impairment. Halflife 7-20 hours | Caution with decreased kidney function |

# PHENTERMINE

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR<br>BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| weight loss (WL) | Variable, >5.5 kg or 7.4% at 12 weeks | |
| Responder rates | ≥5% wt loss: 49-82%<br>≥10% wt. loss: 16-76% | |
| Contraindications | Pregnancy, acute CHD, closed angle glaucoma | |
| Adverse Drug Reactions | Dry mouth, insomnia, constipation, bruxism, palpitations, difficulty with urination, headache, irritability, dysphoria, change in libido | Adverse reactions when given with MAOI, alcohol |

# DIETHYLPROPION

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Dosage | Tenuate® is 25 mg, Tenuate Dispan® is 75 mg ER | Short-acting 4-6 hours and typically TID dosing is used. ER is used daily; DEA schedule IV |
| Mechanism of action (MOA) | Weaker sympathomimetic amine than phentermine and structurally similar to bupropion | |
| Pharmacokinetics | Excreted primarily via urine | Use with caution with renal impairment, no FDA guidance |
| Adverse Drug Reactions | Similar to phentermine | |

# PHENDIMETRAZINE

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Dosage | Phendimetrazine 35 mg (Bontril PDM®), Phendimetrazine ER 105 mg (Bontril Slow Release®) | Often prescribed 2-3x daily 1 hour before meals;<br>DEA schedule III; some will use off label in PM with Am phentermine |
| Mechanism of action (MOA) | Weaker sympathomimetic amine than phentermine | |
| Pharmacokinetics | Excreted primarily via urine | Half life is ~3.7 hours; no FDA guidance on impaired renal function, use with caution |
| Adverse Drug Reactions | Similar to phentermine | |

# BENZPHETAMINE

| Indications | Chronic Obesity Management | BMI≥30kg/m2 OR BMI≥27kg/m2 with at least one weight-related comorbidity |
|---|---|---|
| Dosage | 25-50 mg by mouth once daily | may increase to 25 to 50 mg 1 to 3 times daily based on response and tolerability |
| Mechanism of action (MOA) | Sympathomimetic amine similar to phentermine | |
| Adverse Drug Reactions | Similar to phentermine | |

## AVOID SYMPATHOMIMETICS if…

- Pregnancy or planning to become pregnant (cat. X)
- Nursing mothers/Lactation (cat. X)
- Already experience the ADRs
- Advanced or Symptomatic CAD 5. Uncontrolled Hypertension
- Hyperthyroidism
- Closed Angle Glaucoma
- Severe Anxiety or other Uncontrolled Mental Health
- Hypersensitivity to ingredients
- Drug Interactions: MAO inhibitor use within 14 days, Anesthesia
- Nutrient Interaction: Caffeine, Alcohol

## Consider DISCONTINUING SYMPATHOMIMETICS if…

- COMMON SIDE EFFECTS:
- Constipation
- Diarrhea
- Dry Mouth (Mucosal Erosions 1/1000)
- Difficulty Sleeping
- Dizziness
- Dysgeusia
- Decreased Libido
- CNS Overstimulation (Feeling Nervous “Anxiety”/Restless)
- Glaucoma or increased IOP
- Headache
- Increased Blood Pressure
- Heart racing
- Heart Palpitations

# OFF LABEL USE AOMS FOR LONG TERM USE

METFORMIN

TOPIRAMATE

ZONISAMIDE

BUPROPION

SGLT2 INHIBITORS

# OFF LABEL USE AOMS FOR LONG TERM USE

GLP1RA not FDA approved specifically for Obesity

Amylin Agonist (Pramlinitide)

# SPECIAL POPULATIONS BY DIAGNOSIS

- Depression – Bupropion (might be first choice in patients with obesity)
- Binge eating disorder –Lisdexamfetamine is FDA approved for the treatment of moderate to severe binge eating disorder. Topiramate, Duloxetine, Fluoxetine, Bupropion are used off-label
- Night eating syndrome – sertraline, citalopram, escitalopram
- Diabetes: best choices for obesity management include metformin, GLP1 agonists, SGLT2 inhibitors, glucosidase inhibitors; weight neutral: DPP4 inhibitors
- Premenstrual carbohydrate cravings: spironolactone in latter half of cycle to second day of menses. Precaution with patients who may become pregnant. Scant medical literature regarding this treatment (Wang et al. 1995)

# SPECIAL POPULATIONS : PEDIATRICS

**Pediatric population (2 to <12 yo)**

**No AOMs are FDA approved for weight loss in this age range, EXCEPT for Setmelanotide (age6y)**

- Metformin used off-label for PCOS > 10 yo & on-label for T2DM > 10 yo, but if used for obesity is off-label.
- Liraglutide for T2DM > 10 yo

**FDA approved AOM use in Adolescents:**

- Liraglutide ≥ 12 yo (Long term use): Weight > 60 kg or BMI equivalent ≥ 30 kg/m² for age using Cole criteria
- Phentermine for > 16 yo (FDA-approved for short term use)
- Orlistat for > 12 yo (Long term use)

# SPECIAL POPULATIONS : GERIATRICS

Geriatric population (>65 yo):

FDA approved AOMs do not have upper limits of age for use

*Clinical trials did not enroll large groups of these patients

*Take into account their concomitant disease states, drug interactions, and renal function for dose adjustments, if needed

# SPECIAL POPULATIONS : PREGNANT WOMEN

## FDA Approved AOMS are C/I in PREGNANCY

| Medication | Pregnancy Category | Cessation before contraception |
|---|---|---|
| Phentermine | X | 2 weeks |
| Phen/Top (Qsymia) | X | 3 months |
| Bup/Nal (Contrave) | X | |
| Liraglutide | C | |
| Semaglutide | | 2 months |
| Orlistat | B | |
| Diethylpropion | B | |
| Phendimetrazine | X | |

# CONTRAINDICATIONS FOR OBESITY TREATMENT

| C/I | | | | |
|---|---|---|---|---|
| Brain Fog /Depression | Topiramate* | Zonisamide* | | |
| CVD /Uncontrolled HTN/ Hyperthyroidism | Qsymia* | Phentermine* | Diethylpropion* | |
| Depression | Topiramate* | Zonisamide* | | |
| Gastroparesis | Liraglutide | Semaglutide | | |
| Glaucoma** | Qsymia* | Phentermine* | Diethylpropion* | Zonisamide |
| Nephrolithiasis** | Topiramate* | Orlistat | | |
| Paresthesias | Topiramate* | Zonisamide* | | |
| Seizures | Bupropion | Diethylpropion* | | |
| Vit D deficiency | Orlistat | | | |
| * Relative C/I | ** depends on type | | | |

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