

# Anti-Obesity Medications (AOMs)

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Heartland Weight Loss



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## Disclaimer

- The following educational materials are based on peer reviewed research, extensive clinical experience, advanced certification and risk stratifying to the needs of each patient.
- The educational content and case studies are meant to serve as a primer to inform the primary care team of the complex nature of obesity management as a chronic disease.
- Additional details and references are provided in the companion handout. For full prescribing information see package inserts.



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## Outline

- Purpose of AOMs
- FDA-Approved for Long-term Use
- FDA-Approved for Short-term Use
- Off-Label Use
- Case Studies
- Handout Guide



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## Purpose of AOMs

- Treatment of excess weight and related comorbidities - along with lifestyle interventions
- Slow progression of weight regain
- Used in sequence or in combination with bariatric surgery
- Improve health and QOL

Bays, H. E., Fitch, A., Christensen, S., BurrIDGE, K., & Tondt, J. (2022). Anti-obesity medications and investigational agents: An obesity medicine association (OMA) clinical practice statement (CPS) 2022. Obesity Pillars, 2. <https://doi.org/10.1016/j.obpill.2022.100018>.



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# Indications for Use of Anti-Obesity Medications (AOMs)

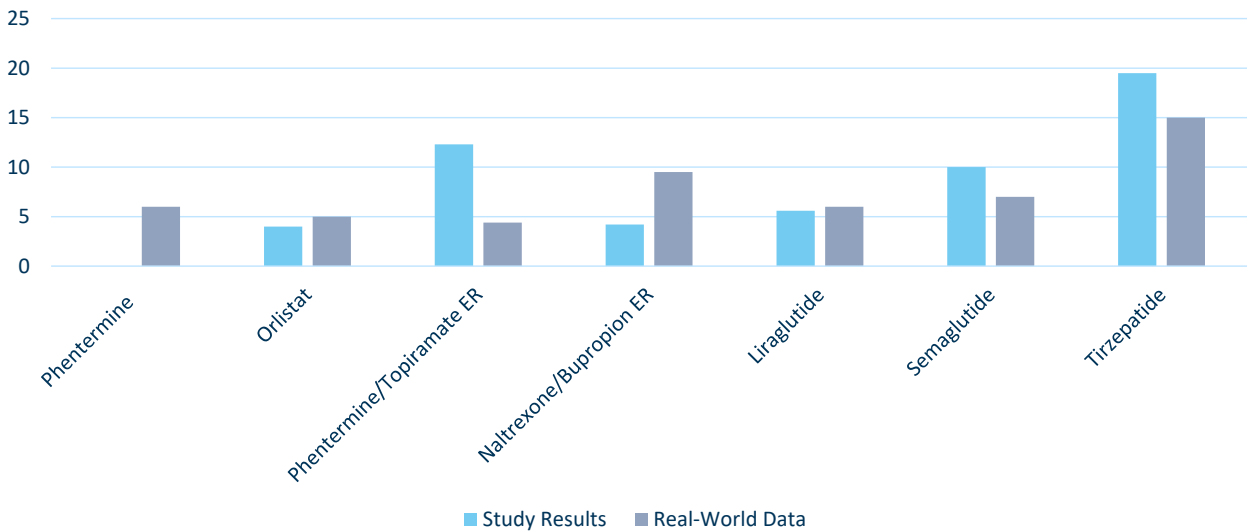
| Treatment                                    | BMI Category |                     |                     |         |     |
|--|--------------|---------------------|---------------------|---------|-----|
|  | 25-26.9      | 27-29.9             | 30-34.9             | 35-39.9 | ≥40 |
| Diet, Physical Activity & Behavioral Therapy | +            | +                   | +                   | +       | +   |
| Pharmacotherapy                              |              | with co-morbidities | +                   | +       | +   |
| Bariatric Surgery                            |              |                     | with co-morbidities |         | +   |

Apovian, et al. Pharmacological management of obesity: An Endocrine Society clinical practice guideline. The Journal of Clinical Endocrinology & Metabolism, 100(2), 342-362.



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% Average Weight Loss (Drug Minus Placebo)



Arrone et al 2013, EQUIP trial, BMOD trials, SURMOUNT trial, STEP trial.



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## AOMs FDA-Approved for Long-term Use

### Orlistat

Trade Name: Xenical, Alli®

### Phentermine/ Topiramate ER

Trade Name: Qsymia®

### Naltrexone/ Bupropion ER

Trade Name: Contrave®

### Liraglutide

Trade Name: Saxenda®  
(Victoza® off label)

### Semaglutide

Trade Names: Wegovy®  
(Ozempic® off label)

### Tirzepatide

Trade Name: Zepbound  
(Mounjaro® off label)



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## Orlistat

Xenical® / alli®

- MOA
  - Gastrointestinal lipase inhibitor, prevents absorption of ~ 30% of ingested fat
- Contraindications
  - Pregnancy/nursing, chronic malabsorption syndrome, cholestasis
- Common AEs
  - Diarrhea, oily stools, fecal incontinence
- Mean Weight Loss
  - 9% (vs. placebo: 6%)
- Considerations
  - Inexpensive / available OTC
  - No central side effect profile
  - FDA approved for long-term use
- Best Candidates
  - \$\$



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## Phentermine/Topiramate ER

Qsymia®

- MOA
  - Combination stimulant and anticonvulsant. Decreases appetite/increases satiety and possibly affects resting energy expenditure. Exact MOA unknown.
- Contraindications
  - Pregnancy / Nursing
  - History of CVD (CAD, stroke, arrhythmias, CHF, uncontrolled HTN)
  - Hyperthyroidism
  - Narrow angle glaucoma
  - Agitated states
  - History of drug abuse (schedule IV drug)
- Common AEs
  - Paresthesia, dizziness, dysgeusia, insomnia, constipation, dry mouth, disturbance in attention.

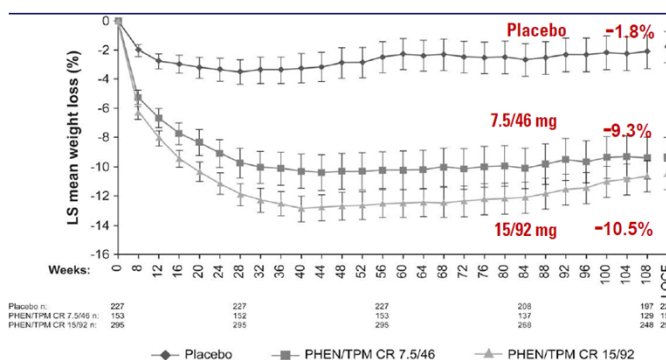


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## Phentermine/Topiramate ER

Qsymia®

- Mean Weight Loss
  - 9% - 10% (vs. 2% placebo)
- Considerations
  - Highly effective
  - Higher level of monitoring required for drug interactions and AEs
- Best Candidates
  - \$\$ (can get discounts down to \$98/month)
- Clinical Pearls
  - Women not at risk of pregnancy, people w/ no CV disease, people with food/sugar cravings (esp soda)



Am J Clin Nutr. 2012; 95:297-308.



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## Naltrexone/Bupropion HCL ER Contrave®

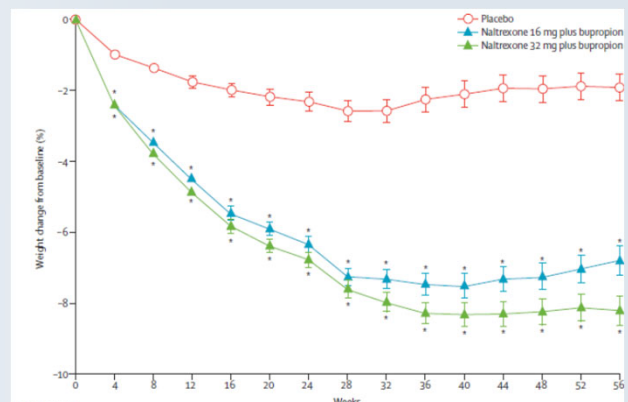
- MOA
  - Combination antidepressant/opioid antagonist. Decreases appetite and reward response. Exact MOA not fully understood.
- Contraindications
  - Uncontrolled HTN
  - Seizure disorder
  - Narrow angle glaucoma
  - Bipolar mood disorder
  - Anorexia nervosa or bulimia
  - Chronic opioid use
  - During or within 14 days of taking monoamine oxidase inhibitors
- AEs
  - Common: nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea



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## Naltrexone/Bupropion HCL ER Contrave®

- Mean Weight Loss
  - 7% (v. 2% placebo)
- Considerations
  - Higher level of monitoring required for drug interactions and AEs
  - Additional benefits: EtOH cessation, smoking, depression, excessive cravings, reward pathway, hedonic eating
- Potential Candidates
  - \$\$ (can get for \$99/month with Contrave program)
- Clinical Pearls
  - People who are not candidates for medications containing a stimulant
  - May benefit boredom, emotional and nighttime eaters.

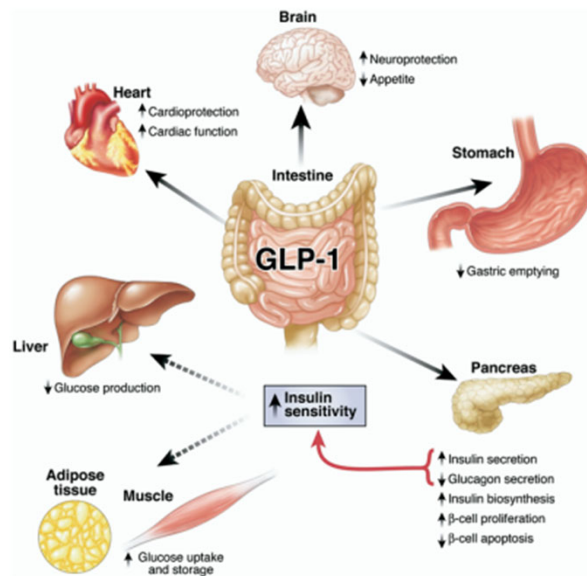


Lancet 2010; 376:595-605.



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## GLP-1 Receptor Agonists



Gastroenterology 2007; 132:2131-2157.



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## GLP-Receptor Agonists

- AEs
  - Nausea, constipation, diarrhea, headache, vomiting, injection site reaction, hypoglycemia, dyspepsia, fatigue, dizziness, abdominal pain, increased lipase levels
- Contraindications
  - Pregnancy or nursing
  - Personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome type 2
- Considerations
  - Additional benefits: diabetes treatment, improves BP, cardiovascular data, lack of central side effects, high efficacy
- Best Candidates
  - Patients with Type 2 diabetes
  - Those who can afford the medications



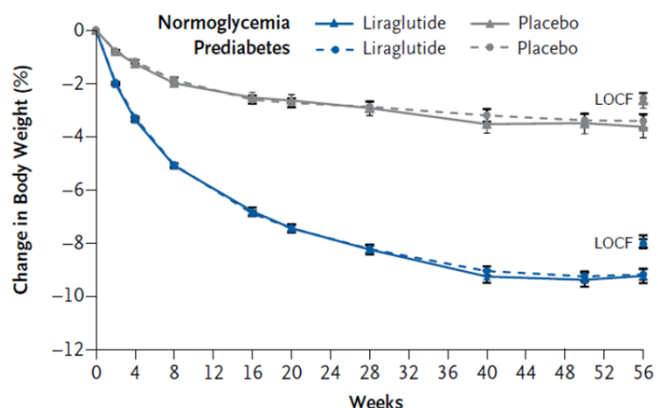
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## Liraglutide

Saxenda®



- Mean Weight Loss
  - 8% (v. 3% placebo)
- Considerations
  - Daily injection
  - Titrate dose every 7 day up to max of 3 mg
  - \$\$\$\$



Pi-Sunyer X, et al. A Randomized, Controlled Trial of 3.0 mg of Liraglutide in Weight Management. N Engl J Med. 2015 Jul 2;373(1):11-22.



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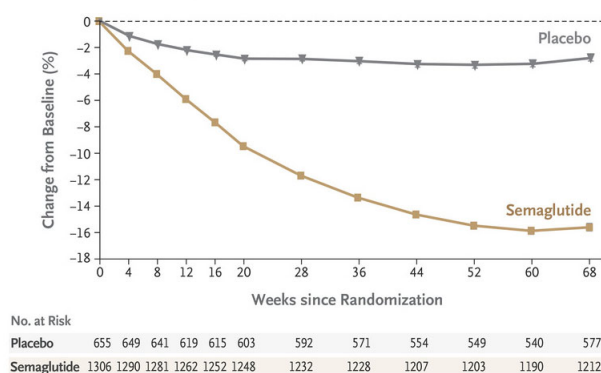
## Semaglutide

Wegovy®



- Mean Weight Loss
  - 15% (v. 2% placebo)
- Considerations
  - Weekly injection
  - Titrate dose every month up to max of 2.4 mg
  - \$\$\$\$

Body Weight Change from Baseline by Week, Observed In-Trial Data



Wilding JPH, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med. 2021 Mar 18;384(11):989-1002.



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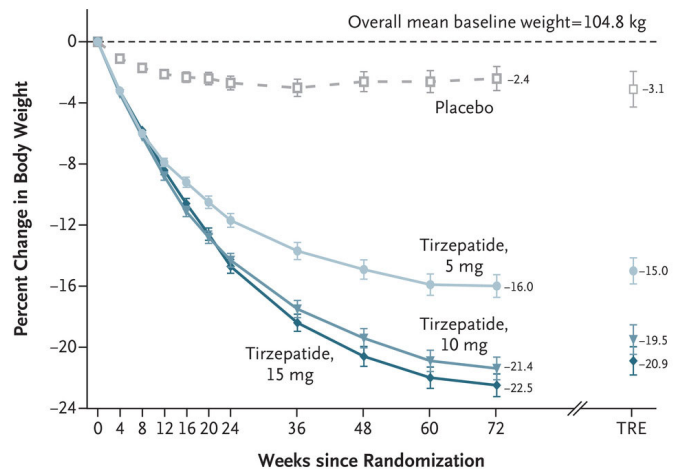


## Tirzepatide

Zepbound®



- AEs
  - Similar to GLP-1 agonists
- Mean Weight Loss
  - 21% (vs. placebo 3%)
- Considerations
  - \$\$\$\$



Jastreboff AM, et al. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med. 2022 Jul 21;387(3):205-216.



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## GLP-1 Access

- Figuring out coverage is trial and error
  - Patients can check with insurance company first
  - Write Rx, fill out prior authorization, fill out appeal as needed
- Compounding
  - Compounding pharmacies cannot obtain actual semaglutide/tirzepatide and are not required to have 3<sup>rd</sup> party testing on their products – not recommended
- Self-loading vs. preloaded injections
  - Self-loaded easier to titrate
  - Preloaded less room for error
  - Coverage typically determines choice



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## Considerations for all AOMs

- Successful treatment with AOMs is highly dependent upon concurrent lifestyle modifications around nutrition and exercise
- Weight loss, especially if rapid, can lead to negative body composition changes; therefore, increased protein and resistance training are especially important.



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## FDA Approved AOMs for Short-term Usage

**Diethylpropion or  
Diethylpropion ER**

Trade Names:  
Tenuate®, Tenuate Dospan®

**Phentermine**

Trade Names:  
Lomaira®, Adipex-P®

**Phendimetrazine or  
Phendimetrazine ER**

Trade Names:  
Bontril PDM®, Bontril Slow Release®



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## Noradrenergic Agents

- Options
  - Phentermine (Schedule IV)
  - Diethylpropion (Schedule IV)
  - Phendimetrazine (Schedule III)
- MOA
  - Stimulants decrease appetite/increases satiety and possibly change resting energy expenditure
- AEs
  - Dry mouth, insomnia, constipation, headache, elevations in blood pressure and/or heart rate



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## Noradrenergic Agents

- Contraindications
  - Pregnancy / Nursing
  - History of CVD (CAD, stroke, arrhythmias, CHF, uncontrolled HTN)
  - Hyperthyroidism
  - Narrow angle glaucoma
  - Agitated states
  - History of drug abuse
- Mean Weight Loss
  - 7-10% (v. placebo 2-3%)
- Additional considerations
  - Time tested; highly effective
  - Low cost ~ \$11/month
  - Potential for abuse, but no documented cases
  - Consider EKG to screen for occult cardiac disease

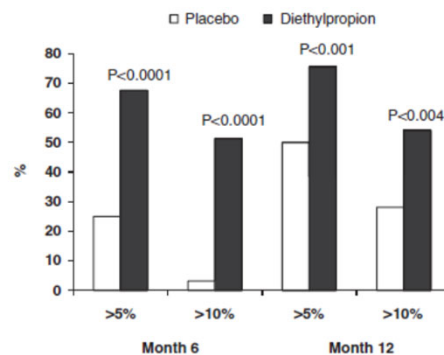


Figure 3 Number of patients achieving weight loss of 5 and 10% according to the group assignment at months 6 and 12. Placebo switched to diethylpropion on open-label phase (months 7–12).



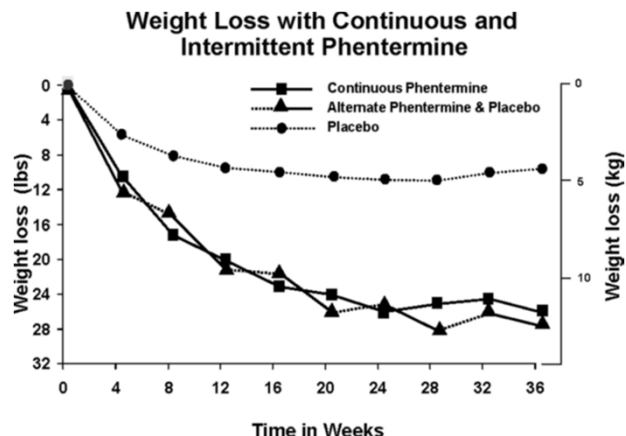
Cercato C, et al. A randomized double-blind placebo-controlled study of the long-term efficacy and safety of diethylpropion in the treatment of obese subjects. *Int J Obes (Lond)*. 2009 Aug;33(8):857-65.



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## Noradrenergic Agents

- Only approved for short-term use (12 weeks)
  - Limited data on long-term safety though phentermine/topiramate has been approved for long-term use
  - Intermittent therapy (figure) is sometimes used
- Best candidates
  - People without contraindications
  - \$



Circulation. 2012;125:1695–1703.



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## Phentermine for Longer Term Use?

- Pros
  - Highly effective and inexpensive
  - Short half-life
  - No documented cases of abuse
  - Safe, but can raise HR and BP slightly / consider EKG
- Challenges
  - KS requires 5% weight loss in first 90 days to qualify for LT treatment
  - 30-day supply only with in person appointment monthly
  - More hurdles with LT treatment during maintenance phase of weight loss



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## Off-Label Use (for Long-Term Use)

### Metformin

Trade Names: Glucophage®,  
Glucophage XR®

### Bupropion

Trade names: Wellbutrin XL®,  
Wellbutrin SR®

### Topiramate

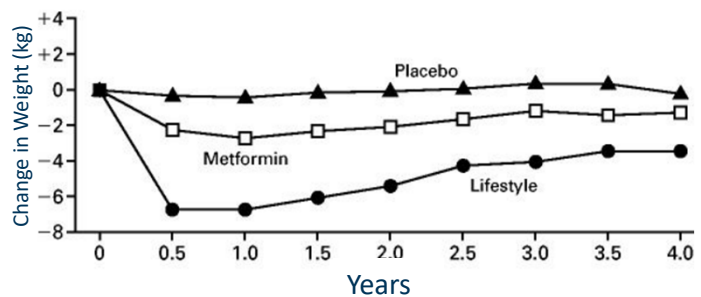
Trade Names: Topamax®,  
Trokenidi XR®



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## Metformin

- AEs
  - Nausea, vomiting, diarrhea, abdominal cramping, Ca<sup>2+</sup> supplementation or avoiding high fat foods may mitigate
- Mean Weight Loss: 2.1 kg at avg 2.8 years of follow-up
- Considerations
  - May help with weight gain related to antipsychotics and HIV meds
  - PCOS, diabetes, pregnancy
- Best candidates
  - Anyone with any degree of insulin resistance



N Engl J Med. 2002 Feb 7; 346 (6): 393-403.



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## Bupropion

- MOA
  - Aminoketone antidepressant with relatively weak inhibition of neuronal reuptake of norepinephrine and dopamine that may work in the hypothalamus and mesolimbic/dopamine circuit to decrease appetite and reward
- Contraindications
  - Uncontrolled hypertension, seizure disorder, narrow angle glaucoma
  - Bipolar mood disorder, anorexia nervosa or bulimia
  - Undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiepileptic drugs
  - During or within 14 days of taking monoamine oxidase inhibitors
- Additional Benefits
  - Tx for depression, smoking cessation



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## Topiramate

- MOA
  - Enhances GABA(A) activity, which may inhibit obesity-promoting neurons
- Contraindications
  - Known hypersensitivity
  - Pregnancy (or likely to become pregnant)
  - Closed angle glaucoma
- Best candidates
  - Tx for migraines, seizures, **binge eating disorder**, bipolar, insomnia, **nighttime eating**



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## AOM Cost Considerations

| Medication                          | Average Monthly Cost w/o Insurance |
|-------------------------------------|------------------------------------|
| Saxenda® (Liraglutide)              | \$1,300                            |
| Wegovy® / Ozempic® (Semaglutide)    | \$1,300 / \$950                    |
| Zepbound® / Mounjaro® (Tirzepatide) | \$1,100                            |
| Qsymia® (Phentermine/Topiramate)    | \$170 (\$75 w/ coupon)             |
| Contrave® (Bupropion/Naltrexone)    | \$500 (\$99 w/ coupon)             |
| Xenical® / Alli® (Orlistat)         | \$278 / \$47 OTC                   |
| Topiramate                          | \$10                               |
| Metformin                           | \$14                               |
| Phentermine                         | \$15                               |

Costs are estimates based on lowest prices available through GoodRx. April 2024.  
Manufacturer may have coupon program available.



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## Anti-Obesity Drug Selection – Clinical Pearls

| Medication                             | Rx Notes  | Why choose this drug?  | Why NOT choose this drug?   |
|--|---|--|---|
| Orlistat                               | Daily to TID  | No central side effect profile   | Less effective, GI side effects, B12 deficiency, \$   |
| Phentermine/ Topiramate ER             | Daily, titrated gradually   | Highly effective   | Stimulant effect, <b>potentially teratogenic</b> , hx of kidney stones or glaucoma, \$\$  |
| Naltrexone-Bupropion HCl XR            | Daily to BID dosing, titrated gradually   | Additional benefits: EtOH cessation, smoking, depression, Excessive cravings, reward pathway, hedonic eating | Nausea, h/o seizures, bulimia, bipolar mood d/o, glaucoma, \$\$   |
| GLP-1 RAs: Liraglutide and Semaglutide | Liraglutide daily<br>Semaglutide weekly, both subcutaneous administration, titrated gradually | Additional benefits: diabetes, Improves BP, cardiovascular data, lack of central side effects, high efficacy | Personal/family h/o medullary thyroid carcinoma or MEN-2, gastroparesis, pancreatitis, planning pregnancy soon (women only), \$\$\$\$ |



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## Anti-Obesity Drug Selection – Clinical Pearls

| Medication  | Rx Notes  | Why choose this drug?   | Why NOT choose this drug?   |
|---|---|---|---|
| <b>Phentermine, Diethylpropion, Phendimetrazine</b> | Daily to BID (TID with 8mg dose of phentermine) | Time tested, highly effective   | Stimulant effect, cardiac disease, uncontrolled HTN, glaucoma, anxiety controlled substance, \$                           |
| <b>Plenity</b>                                      | BID (prior to lunch and dinner)                 | Not systemically absorbed   | GI side effects, h/o esophageal anatomic abnormalities, history of GI surgery complications that may alter motility, \$\$ |
| <b>Topiramate</b>                                   | Daily to BID, can titrate                       | Additional benefits: migraines, seizures, binge eating disorder, bipolar, may help insomnia, may change the taste of foods, especially soda | Cognitive impairment, parasthesias, teratogenic effect (planning to be pregnant), h/o nephrolithiasis, \$                 |



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## Anti-Obesity Drug Selection – Clinical Pearls

| Medication         | Rx Notes                                       | Why choose this drug?   | Why NOT choose this drug?   |
|--------------------|--|---|---|
| <b>Bupropion</b>   | Daily to BID                                   | Additional benefit: depression, smoking cessation   | h/o seizures, bulimia, bipolar mood d/o, \$   |
| <b>Tirzepatide</b> | Weekly subcutaneous injection, titrate monthly | Additional benefit: diabetes, highly effective, less GI side effects than GLP-1 RA                                  | Personal/family h/o medullary thyroid carcinoma or MEN-2, gastroparesis, pancreatitis, planning pregnancy soon (women only), \$\$\$\$ |
| <b>Metformin</b>   | Daily to BID, titrate                          | Additional benefits: PCOS, diabetes, pregnancy, counteract the weight-positivity of the typical anti-psychotic meds | GI side effect profile, potential B12 deficiency, \$  |



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