

# 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., Burrige, 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)

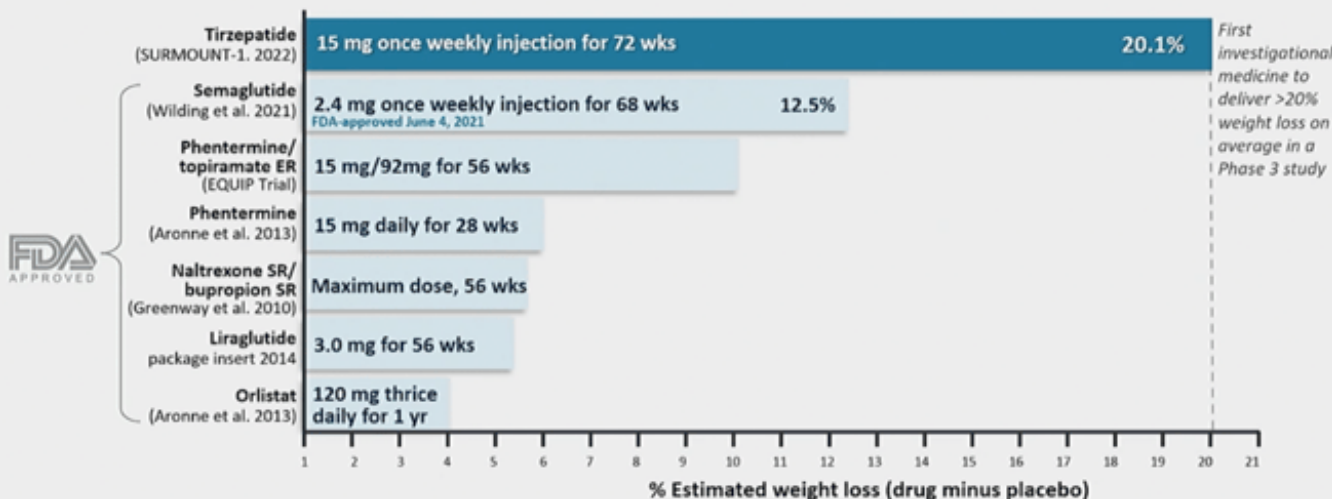
Treatment	BMI Category				
	25-26.9	27-29.9	30-34.9	35-39.9	≥40
Diet, Physical Activity & Behavioral Therapy	+	+	+	+	+
Pharmacotherapy		with co-morbidities	+	+	+
Bariatric Surgery			with co-morbidities		+

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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## Efficacy of Current Anti-obesity Drugs



Indicated to be used as adjuncts to a reduced-calorie diet and increased physical activity for chronic weight management in adults with a BMI ≥30 kg/m<sup>2</sup> or those with a BMI ≥27 kg/m<sup>2</sup> who have at least one weight-related comorbid condition such as diabetes mellitus, hypertension, hyperlipidemia or sleep apnea

Srivastava G and Apovian CM. *Nat Rev Endocrinol.* 2018 Jan;14(1):12-24.

Wilding JPH, et al. *N Engl J Med.* 2021 Mar 18;384(11):989.

Eli Lilly Press Release 4/28/22. Media. Maggie Pfeiffer; monson\_maggie@lilly.com



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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®

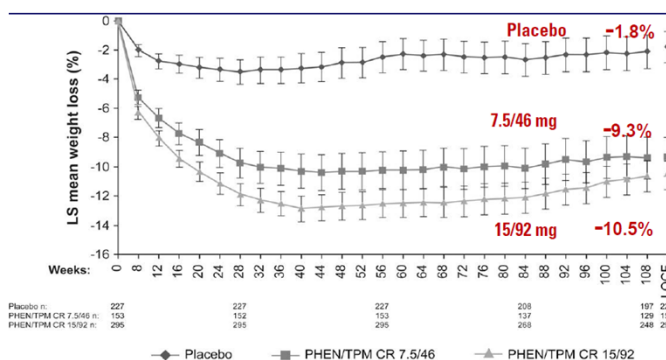
- MOA
  - Combination stimulant and anticonvulsant. Decreases appetite/increases satiety and possibly affects resting energy expenditure. Exact MOA unknown.
- Contraindications
  - Pregnancy / Nursing
  - History of CVD (CAD, stroke, arrhythmias, CHF, uncontrolled HTN)
  - Hyperthyroidism
  - Narrow 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®

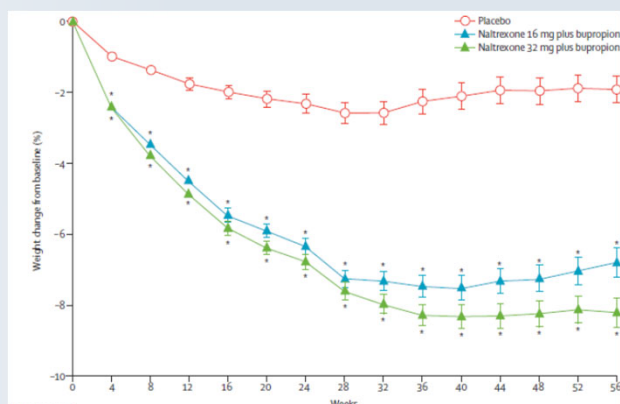
- MOA
  - Combination antidepressant/opioid agonist. Decreases appetite and reward response. Exact MOA not fully understood.
- Contraindications
  - Uncontrolled HTN
  - Seizure disorder
  - Narrow angle glaucoma
  - Bipolar mood disorder
  - Anorexia nervosa or bulimia
  - Chronic opioid use
  - During 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.

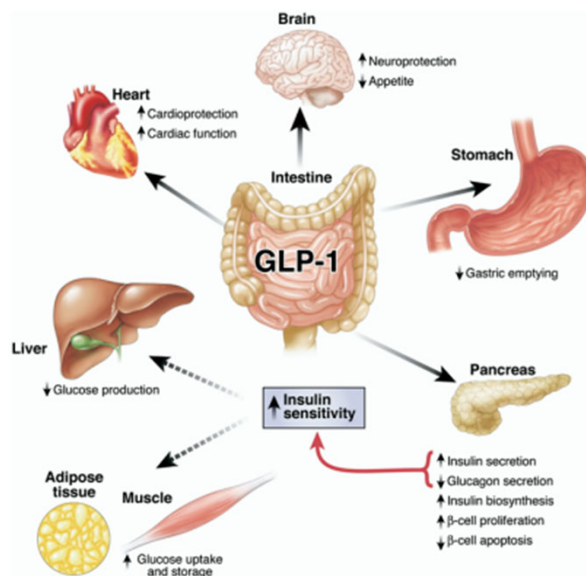


Lancet 2010; 376:595-605.



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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

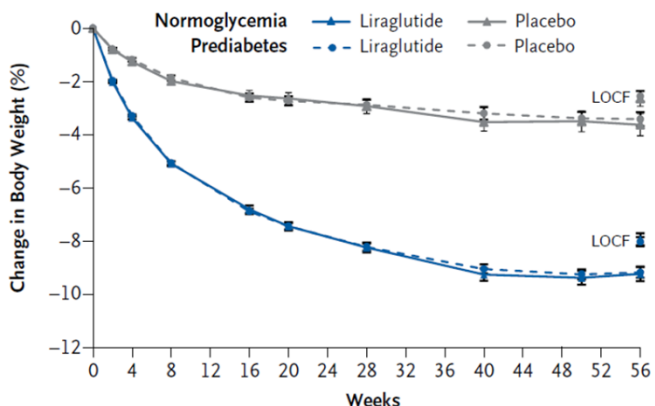


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## Liraglutide Saxenda®



- 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.



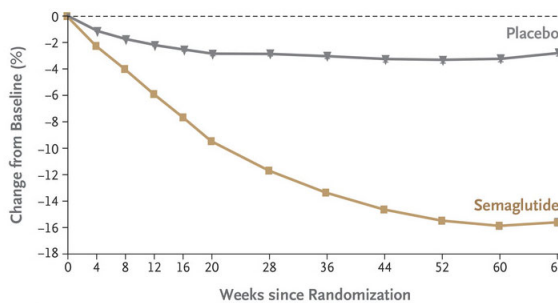
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## Semaglutide Wegovy®



- 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



No. at Risk	0	4	8	12	16	20	28	36	44	52	60	68
Placebo	655	649	641	619	615	603	592	571	554	549	540	577
Semaglutide	1306	1290	1281	1262	1252	1248	1232	1228	1207	1203	1190	1212

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



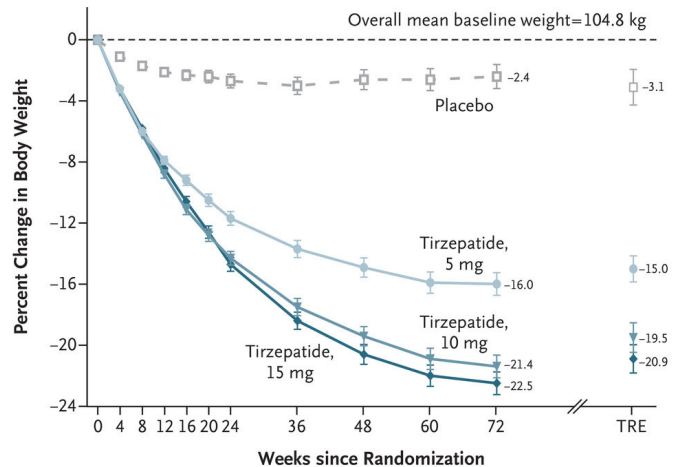
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## Tirzepatide Zepbound®



- 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

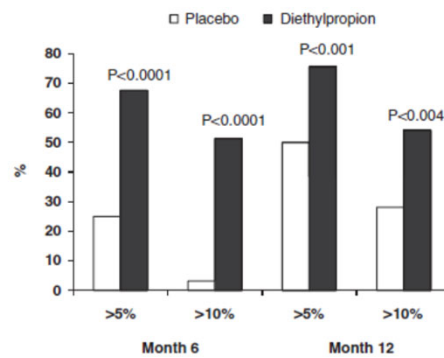


Figure 3 Number of patients achieving weight loss of 5 and 10% according to the group assignment at months 6 and 12. Placebo switched to diethylpropion on open-label phase (months 7–12).



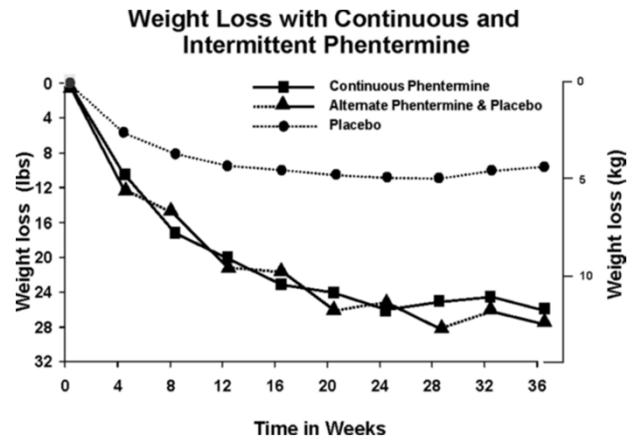
Cercato C, et al. A randomized double-blind placebo-controlled study of the long-term efficacy and safety of diethylpropion in the treatment of obese subjects. *Int J Obes (Lond)*. 2009 Aug;33(8):857-65.



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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.



## 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



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

### Metformin

Trade Names: Glucophage<sup>®</sup>,  
Glucophage XR<sup>®</sup>

### Bupropion

Trade names: Wellbutrin XL<sup>®</sup>,  
Wellbutrin SR<sup>®</sup>

### Topiramate

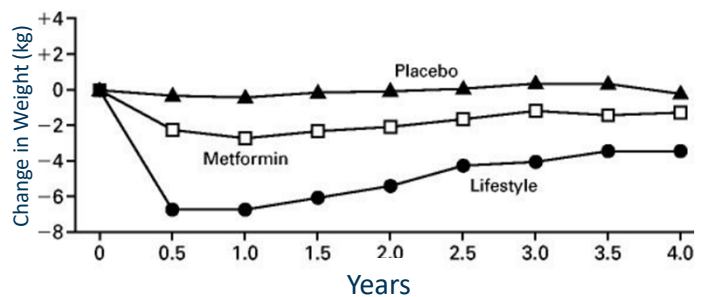
Trade Names: Topamax<sup>®</sup>,  
Trokendi XR<sup>®</sup>



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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 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

Anti-Obesity Drugs	Rx Notes	Why choose this drug?	Why NOT choose this drug?
Phentermine, Diethylpropion, Phendimetrazine	Daily to BID (TID with 8mg dose of phentermine)	Time tested, highly effective	Stimulant effect, cardiac disease, uncontrolled HTN, glaucoma, anxiety controlled substance, \$
Plenity	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, \$\$
Topiramate	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

Anti-Obesity Drugs	Rx Notes	Why choose this drug?	Why NOT choose this drug?
Bupropion	Daily to BID	Additional benefit: depression, smoking cessation	h/o seizures, bulimia, bipolar mood d/o, \$
Tirzepatide	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), \$\$\$\$
Metformin	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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**Questions?**

