

Addressing Obesity A Community of Practice:

Pharmacologic Options for the Treatment of Obesity

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The Obesity Medicine Association's (OMA)
4 PILLARS OF CLINICAL OBESITY TREATMENT

Nutrition

Physical Activity

Behavior

Medication

Successful + Sustainable Weight Loss = A Comprehensive, Evidence-Based Approach

Obesity Medicine Association. Accessed July 24, 2023. <https://obesitymedicine.org/press-four-pillars-the-fundamentals-of-obesity-management-and-treatment/>


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Check for Obesogenic Medications

- Diabetes (insulin, sulfonylureas, TZDs, meglitinides)
- Hormones
- Anti-inflammatory medications
- Anti-seizure medications
- Antidepressants (especially TCAs and mirtazapine)
- Antipsychotics & mood stabilizers
- CV (beta blocker, CCB)
- Migraine medications
- Hypnotics
- Antihistamines
- Steroids
- HIV medications
- Chemotherapy medications
- Organ transplant medications

TZD, thiazolidinedione; TCA, tricyclic antidepressant; CV, cardiovascular; CCB, calcium channel blocker.
Whitton S, et al. Obesity Med. 2016; 1(1):47-58.


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Why Use AOMs as Part of Treatment 

- Medications are adjunct with lifestyle
- Medications help people accomplish lifestyle changes and make them durable/sustainable
- Some patients are adamantly opposed to bariatric surgery but may consider medication
 - Some newer medications approach effectiveness of surgery

AOM, anti-obesity medication.

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Why Use AOMs as Part of Treatment¹⁻³ 

Initiate Lifestyle Intervention

Patients with overweight or obesity but no weight-related complications

Patients with overweight or obesity and mild to moderate weight-related complications when lifestyle therapy is anticipated to achieve sufficient weight loss to improve the complication (may also consider AOMs at this stage)

Initiate AOMs as an Adjunct to Lifestyle Intervention


Inadequate response to lifestyle intervention

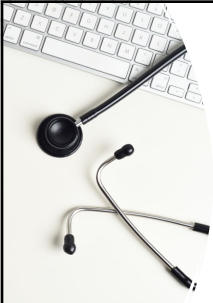
Weight regain after initial weight loss with lifestyle intervention alone

Presence of weight-related complications, particularly if severe, with the intent to achieve sufficient weight loss to ameliorate the complication

BMI, body mass index.
1. Garvey, et al. Endocr Pract. 2016;22(1-2):22-3. 2. Grunwell E, et al. Gastroenterol. 2022;153(5):1108-1225. 3. Apolzan DM, et al. JGIM. 2015;30(2):240-242.

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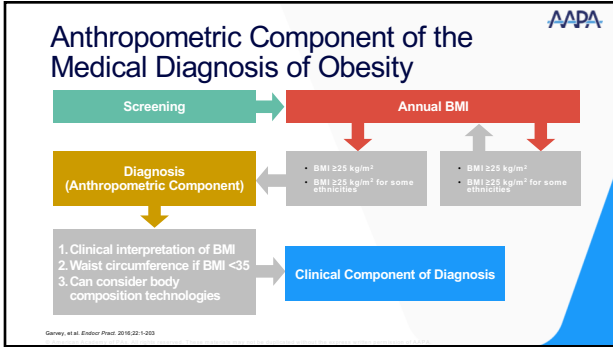
FDA-approved Anti-obesity Medication Indications 



- Patients with obesity (e.g., BMI >30kg/m²)
- Patients with overweight (e.g., BMI 27kg/m²) with presence of a weight-related complication (e.g., type 2 diabetes mellitus, hypertension, dyslipidemia)
- Adjunct to reduced calorie diet and increased physical activity
- Contraindicated in patients hypersensitive to the drugs

BMI, body mass index.
Brand HE, et al. Obesity Algorithm eBook, sponsored by the Obesity Medicine Association. www.obesityalgorithm.org. 2023.

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FDA-approved Anti-obesity Pediatric Medication Indications

Pediatric patients aged 12 years and older with an initial BMI at the 95th percentile or greater for age and sex (obesity)

Ryan HE, et al. Obesity Algorithm eBook, sponsored by the Obesity Medicine Association. www.obesityalgorithm.org. 2023.

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Anti-Obesity Medications

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Medications FDA Indicated for Short-term Use

- Sympathomimetic Amines
 - Phentermine (DEA Schedule IV); 15 mg, 30 mg, 37.5 mg (cap), 8 mg, 37.5 mg (tab)
 - Diethylpropion (DEA Schedule IV) 25 mg, 75 mg ER
 - Phendimetrazine (DEA Schedule III) 35 mg tab, 105 mg ER cap
 - Benzphetamine (DEA Schedule III) 25 mg, 50 mg
- Indication: Short-term use (a few weeks) as adjunct to a weight reduction regimen
- MOA: Norepinephrine-releasing agent; anorexic agent
- Weight Loss Efficacy: 3-8% in controlled clinical trials; 4-19% in retrospective medical chart reviews

MOA, mechanism of action.
Coronel, M. Am. J. Manag. Care. 2022;28(Suppl 1):S288-S296.

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Medications FDA Indicated for Short-term Use

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|---|--|
| <p>Potential Adverse Reactions¹</p> <ul style="list-style-type: none"> • Palpitation • Tachycardia • Increased blood pressure • Overstimulation • Tremor • Dizziness • Insomnia • Dysphoria | <p>Contraindications/Cautions²</p> <ul style="list-style-type: none"> • Headache • Dryness of mouth • Dysgeusia • Diarrhea • Constipation • Hypersensitivity & pregnancy/breastfeeding • History of cardiovascular disease (e.g., coronary artery disease, stroke, arrhythmias, congestive heart failure, uncontrolled hypertension) • Administration during or within 14 days following the administration of monoamine oxidase inhibitors • Hyperthyroidism • Glaucoma • Agitated states • History of drug abuse |
|---|--|

¹ Coronel, M. Am. J. Manag. Care. 2022;28(Suppl 1):S288-S296. ² Baya HE, et al. Obesity: Algorithm eBook, presented by the Obesity Medicine Association. www.obesitymedicine.org. 2023.

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Original Article
CLINICAL TRIALS AND INVESTIGATIONS

Obesity

Safety and Effectiveness of Longer-Term Phentermine Use: Clinical Outcomes from an Electronic Health Record Cohort

Kristina H. Lewis^{1,2}, Heidi Fischer³, Jimmy An⁴, Lee Barrow⁵, Daniel H. Beniszek⁶, Matthew F. Dalrymple⁷, Jay Desai⁸, Stephanie L. Figueroa⁹, Michael Horberg¹⁰, Corinna Kuchnick¹¹, Caryn Oshiro¹², Ayar Yamamoto¹³, Deborah R. Young¹⁴, and David E. Arterburn¹⁵

Lewis KH, et al. Obesity (Silver Spring). 2019;27(4):591-602

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Longer-term Phentermine Use

13,972 adults with phentermine use 2010-2015

- Short-term (reference group)
- Short-term intermittent
- Medium-term continuous
- Medium-term intermittent
- Long-term continuous

Effectiveness

- Percent change in weight from baseline at 6, 12, 24 months

Safety

- Change in blood pressure
- CV Risk-incidence of myocardial infarction, stroke, angina, CABG, carotid artery intervention, or death

CABG, coronary artery bypass graft
Lewin KH, et al. Obesity (Silver Spring). 2019;27(6):1011-1022

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Longer-term Phentermine Use: Key Results

Efficacy

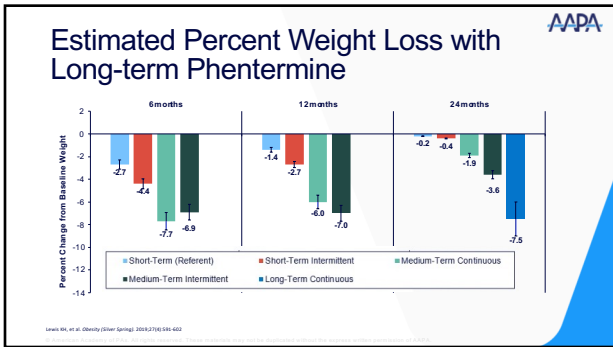
- Longer duration of phentermine use associated with clinically significant greater weight loss up to 2 years
- Discontinuation consistently resulted in weight regain
- Early responders (3% weight loss by 3 months) more likely to reach clinically significant weight loss by 6 months and generally had more durable weight loss in all groups

Safety

- Slight increase in average HR that normalized with drug discontinuation
- No blood pressure difference in groups at 6 months; lower blood pressure noted in comparison groups at 12 and 24 months
- No significant difference in risk of incidence of CVD or death between groups related to duration of phentermine treatment (3-year follow-up)

HR, heart rate; CVD, cardiovascular disease
Lewin KH, et al. Obesity (Silver Spring). 2019;27(6):1011-1022

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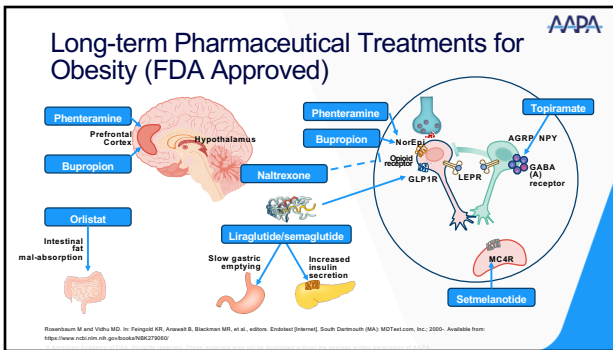


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Long-term Pharmaceutical Treatments for Obesity (FDA Approved)

| Drug Name | Indication | Mechanism of Action | Route |
|----------------------------------|---|---|--------------------|
| Phentermine/topiramate ER | Age 12 years and up | Sympathomimetic, anorectic, reduces appetite | Oral |
| Orlistat | Age 12 years and up (Rx) Age 18 years and up (OTC) | GI lipase inhibitor to decrease fat absorption | Oral |
| Naltrexone/bupropion | Age 18 years and up | Reduces appetite (NDR1) and cravings (opioid antagonists) | Oral |
| Liraglutide | Age 12 years and up, with or without T2DM | GLP-1 receptor agonist, reduces appetite and food intake | Injection (daily) |
| Semaglutide | Age 12 years and up, with or without T2DM | GLP-1 receptor agonist, reduces appetite and food intake | Injection (weekly) |
| Setmelanotide | Age 6 years and up with monogenic or syndromic obesity due to POMC, PCSK1, or LEPR variants | Melanocortin 4 receptor agonist, reduces appetite | Injection (daily) |
| Nonsystemic Oral Hydrogel | Age 18 years and up | Cellulose/citric acid hydrogel, promotes fullness in stomach (device) | Oral |

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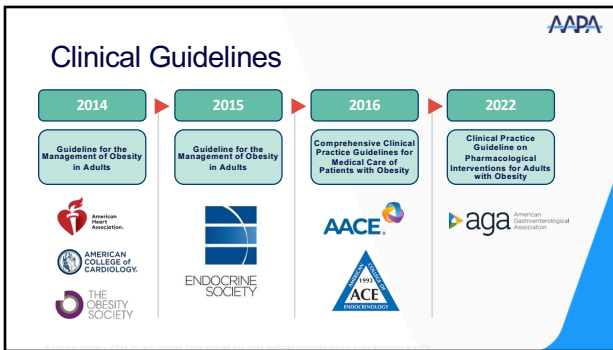
Phentermine/topiramate ER¹⁻⁵

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|--|--|
| Adult dosing | <ul style="list-style-type: none"> Initiate treatment at 3.75 mg/23 mg for 2 weeks Increase to 7.5 mg/46 mg Escalate to 11.25 mg/69 mg for 2 weeks then to max 15 mg/92 mg |
| Efficacy | <ul style="list-style-type: none"> 10% mean weight loss with treatment vs 2% placebo Improved cardiometabolic markers Reduced progression to T2DM |
| Contraindications/ precautions/warnings | <ul style="list-style-type: none"> Monitor for reduced sweating/increased body temp Pregnancy test (baseline & monthly) due to birth defect risk Worsening depression/suicidal thoughts |
| Side effects | <ul style="list-style-type: none"> Increased BP and HR Do not use: pregnancy, glaucoma, hyperthyroid Paraesthesia, dizziness, dysgeusia, insomnia, constipation, dry mouth 1/14 discontinuation rate |
| Clinical considerations | <ul style="list-style-type: none"> Must be discontinued gradually to avoid increased seizure risk Monitor kidney function Taper doses if necessary to discontinue |
| Cost | <ul style="list-style-type: none"> \$200/month for brand name |

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Practical Applications

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Key Pharmacological Guidance

- Add AOM if inadequate response to lifestyle interventions alone
- Early weight loss helps predict sustained weight loss
 - 2.5% weight loss within 1 month for all patients
 - 5-10% within 6 months
- Medication selection is individualized based on treatment goals, weight-related complications, drug cautions and warnings

Medication should be used chronically; short-term treatment is not recommended

Cornier, M. Am J Manag Care. 2022;28(Suppl 11):S288-S296.

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Specific Medication Guidance AAPA

Prioritize semaglutide 2.4 mg due to magnitude of net benefit

- Most current AOM FDA indicated for long-term use have a balance of weight loss over harm that favor their use
- Orlistat – AGA suggests against use; endorsed in older guidelines
- Phentermine
 - AAACE/ACE recommend against off-label AND short-term use
 - Endocrine Society and AGA provide conditional endorsement for off-label use

Avoid off-label use of drugs approved for other disease states for the sole purpose of weight loss

AGA, American Gastroenterological Association; AAACE, American Association of Clinical Endocrinologists; ACE, American College of Endocrinology; Centers for Disease Control and Prevention. *JAMA*. 2022;328(10):929-936.

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Pediatric Guidelines: American Academy of Pediatrics AAPA

1998 & 2007 **Expert Committee Recommendations**

2016 **Algorithm for the Assessment and Management of Childhood Obesity**

2023 **Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents with Obesity**

- Immediate intensive treatment
- Intensive health behavior and lifestyle treatment (IHBLT)
- Insufficient response → intensify treatment with pharmacotherapy/surgery
- <12 years insufficient evidence for use of pharmacotherapy for sole indication of obesity
- Ages 8-11 offer pharmacotherapy for specific conditions according to indications, risks and benefits

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Pediatric Medication Guidance AAPA

Obesity Indication 12+ years

- Orlistat
- Liraglutide 3.0
- Phentermine/topiramate
- Phentermine (16+ yrs)
- Setmelanotide (6+ yrs)

*semaglutide

Other Medical Condition Indication

- Metformin: 10+ T2DM
- Exenatide, dulaglutide, liraglutide 1.8: 10+ T2DM
- Topiramate: 2+ seizure, 12+ headache prevention
- Lisdexamphetamine: 6+ ADHD

AAPOS, American Academy of Pediatrics; American Academy of Pediatrics. *Pediatrics*. 2023;151(10).

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Shared Decision-Making for Choosing AOMs

- Involves choosing treatment based on both evidence and patient preferences
- Consider health literacy: information, drawings



Discuss:

- Comorbid conditions
- Desire for childbearing
- Route of medication
- Availability/supply
- Expected length of time to be on medication
- Risks & benefits of each option
- Cost/coverage
- Expectation of lifestyle as adjunct to medications for best success

Reach a decision together

Assala A, et al. Obstet Gynecol. 2021;128(4):652-671


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Choosing an AOM: Cost/Insurance Factors

Cost affected by:

- Brand name vs generic available
- Insurance coverage
 - Employer based
- Coupon cards
- Pharmaceutical company patient assistance programs




Mason Y, et al. Obstet Gynecol. 2021;128(3):440-445

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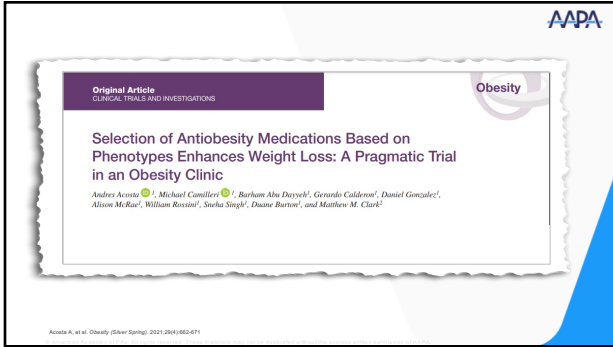
Choosing an AOM: Additional Factors

- Patient preferences**
- Birth control**
- Co-occurring medical conditions**
- Cravings**

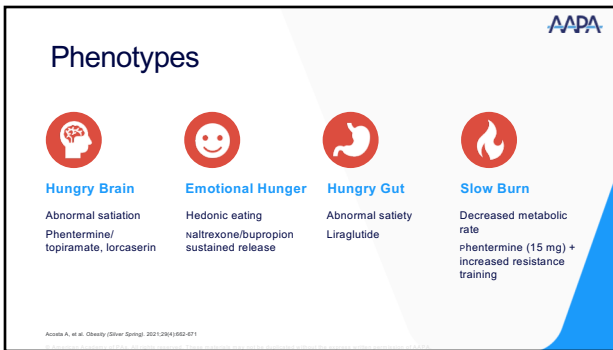


Lari G, et al. Obstet Gynecol. 2021;128(3):440-445

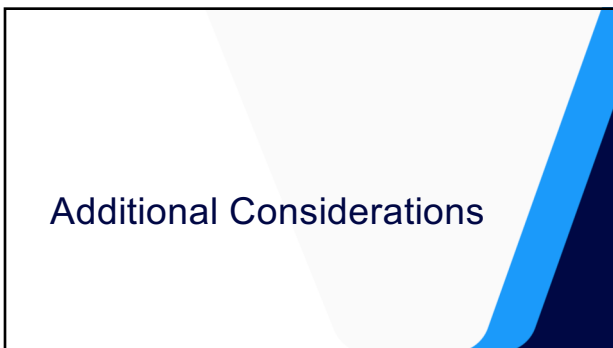
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Anti-obesity Medication: Additional Considerations AAPA

- Medications promote variable weight reduction over variable duration
- If no clinical improvement (3-5% loss of baseline body weight) after 12-16 weeks with one anti-obesity medication, consider alternative medication or increase anti-obesity medication dose (if applicable)
- While BMI is the only measure listed in the prescribing information for anti-obesity medications, BMI has limitations



Boya HE, et al. Obesity Algorithm eBook, presented by the Obesity Medicine Association, www.obesityalgorithm.org, 2023

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FDA-approved Anti-obesity Medication: Additional Considerations AAPA

The decision to continue/discontinue medications without a prescribing information time limitation for use should be based on

- Individual patient response
- Clinical judgment regarding the risk of further/recurrent weight gain



Boya HE, et al. Obesity Algorithm eBook, presented by the Obesity Medicine Association, www.obesityalgorithm.org, 2023

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Medications in Phase 3 Trials¹ AAPA

| | | |
|---|---|--|
| <p>GLP-1/GIP dual agonists</p> <p>Example: tirzepatide</p> | <p>Amylin receptor agonist</p> <p>Example: cagrilintide with semaglutide</p> | <p>SGLT-2 Inhibitors</p> <p>Example: dapagliflozin with metformin</p> |
| <p>Acetylcholine blockers</p> <p>Example: botulinum toxin type A</p> | <p>Dopamine reuptake inhibitor</p> <p>Example: methylphenidate</p> | |

1. Chelloua M, et al. Lancet 2023;58:101882

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Summary AAPA

- ▶ Pharmacotherapy is adjunct to lifestyle as part of a treatment plan
- ▶ All AOMs are contraindicated for use during pregnancy or breastfeeding
- ▶ Obesity is a chronic disease; guidelines help providers decide why, when, and how to use short- and/or long-term medications
- ▶ Patients may be non-responders, early responders, and/or hyper-responders
- ▶ AOM choice is multi-factorial and should be done with patient input and the considerations discussed
- ▶ Research is rapidly evolving, so we will need to keep an eye on the future of AOMs

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Questions

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THANK YOU AAPA

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