Anti-Obesity Medications: How They Work & How to Use Them

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Disclosures

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Objectives

Recognize the role of pharmacotherapy in obesity treatment.

Understand the criteria for patient eligibility for anti-obesity medications.

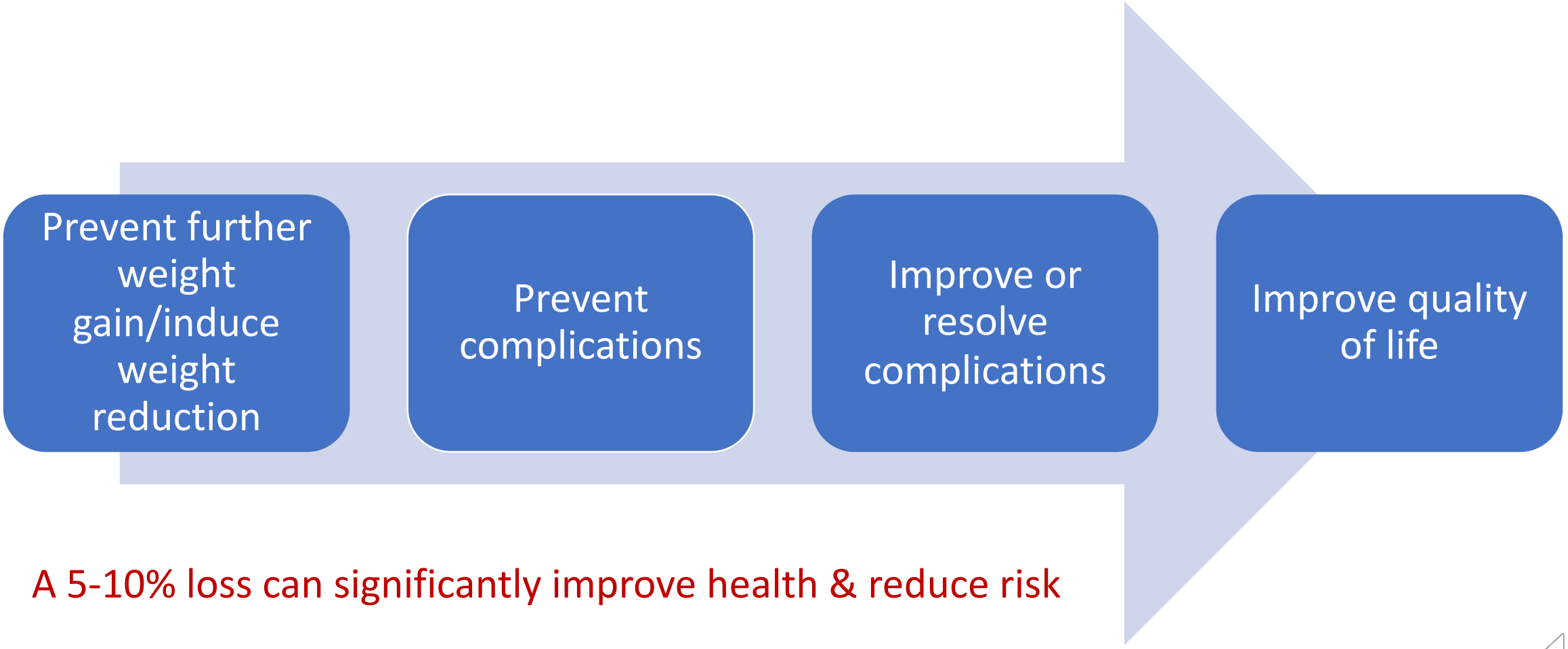
Understand the available FDA-approved anti-obesity medications, including mechanism of action, contraindications, interactions, and adverse effects.

Understand how to personalize medication selection based on mechanism of action

Obesity is a Disease

Obesity is a chronic, progressive, relapsing disease that requires comprehensive long-term treatment

Obesity Treatment Goals



A 5-10% loss can significantly improve health & reduce risk

Comprehensive Treatment Modalities

NUTRITION

PHYSICAL ACTIVITY

BEHAVIORAL THERAPY

PHARMACOTHERAPY

BARIATRIC SURGERY & PROCEDURES

Anti-obesity Medications

Anti-Obesity Medications (AOMs)

Target specific physiology to improve the disease

Work best when they are part of a comprehensive treatment plan that includes:

Nutrition	Physical activity	Behavior modification

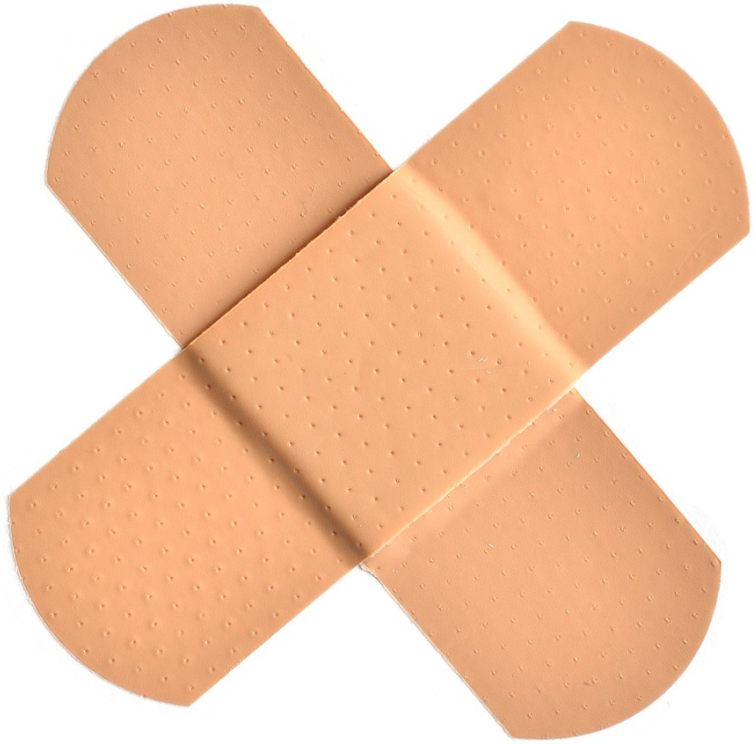
The Purposes of AOMs

Treat	Facilitate	Slow	Improve
Treat the disease of obesity	Facilitate the management of eating behavior	Slow the progression of weight gain & regain	Improve weight, health, & quality of life

Bays, H.E., McCarthy, W., Christensen, S., Tondt, J., Karjoo, S., Davisson, L., Ng, J., Golden, A., Burridge, K., Conroy, R., Wells, S., Umashanker, D., Afreen, S., DeJesus, R., Salter, D., Shah, N. (2020). Obesity Algorithm eBook, presented by the Obesity Medicine Association. https://obesitymedicine.org/obesity-algorithm/

AOMs Are Not

- A Band-Aid
- A crutch
- The easy way out
- The last resort



They are evidence-based tools for treating the disease of obesity

Meet Stephen

46 year-old African American male

PMH

Class III Obesity: BMI 41.6

Prediabetes

Bilateral knee OA

Depression

Current tobacco use

Family History

Father—T2DM, obesity, fatal MI age 62

Mother—prediabetes, obesity, hypertension

Current Meds

Celexa 30 mg daily

Metformin ER 2000 mg daily

Weight history

Has struggled with weight his entire life

Has tried various methods to lose weight. All have been successful, but he always regains the lost weight & is now his highest weight

Rarely feels satisfied after one portion & often goes back for another helping

Loves sweets & finds it difficult to resist them

Who is eligible for AOMs?

FDA Eligibility criteria

- ❖ BMI > 30
- ❖ BMI > 27 with complications such as:
  - T2DM
  - HTN
  - Dyslipidemia
  - OSA

Is Stephen eligible for AOMs?

Which medications are available?

Medications approved for short-term use

- Phentermine
- Diethylpropion
- Phendimetrazine

Medications approved for chronic use

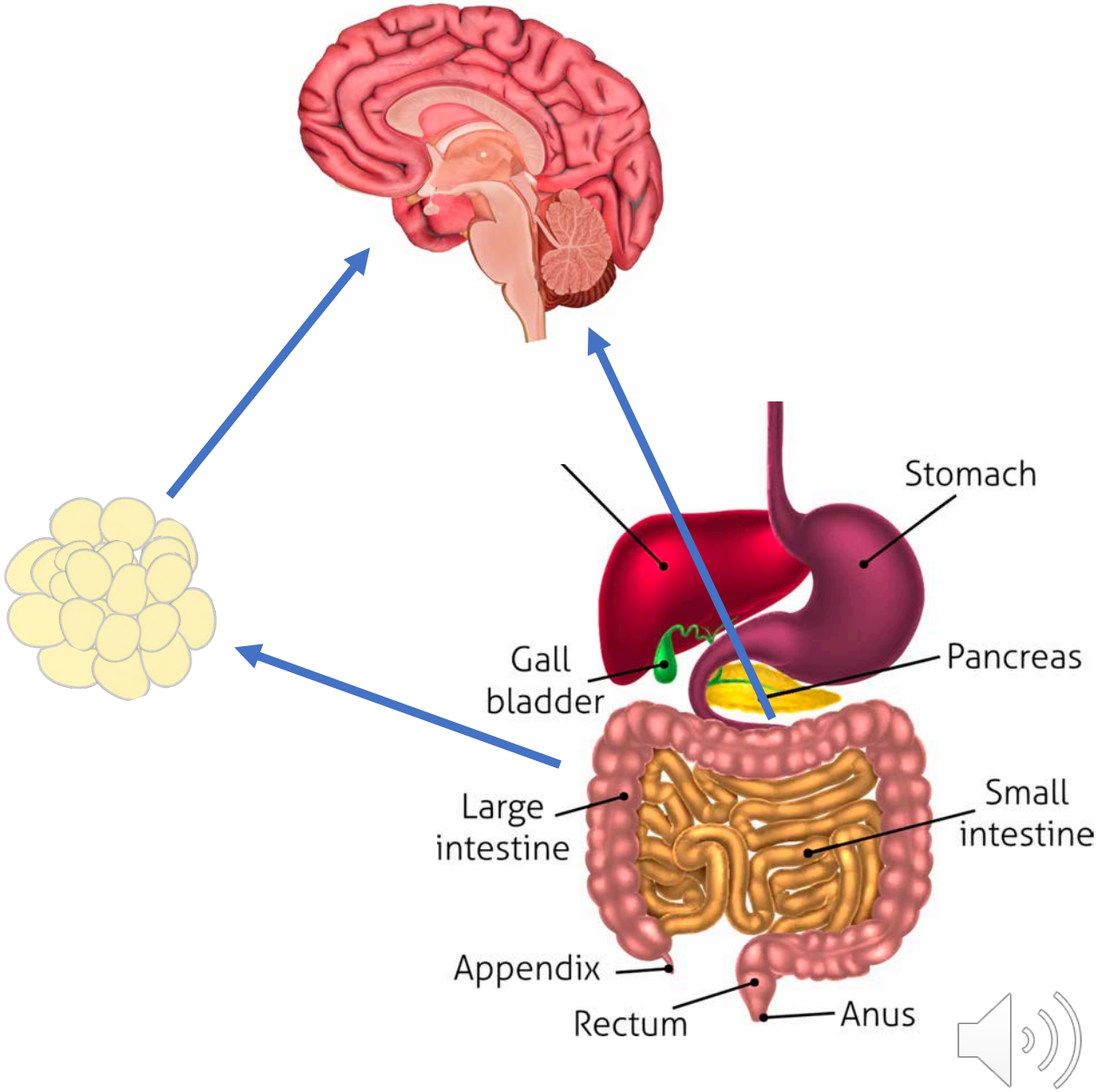
- Orlistat
- Phentermine/topiramate
- Bupropion/naltrexone
- Liraglutide

How do they work?

They work primarily by regulating hormones in the brain, digestive system & adipose tissue to:

- Suppress appetite
- Suppress cravings
- Promote satiety

Each medication has its own specific mechanism(s) of action



Why would a PA choose to prescribe AOMs?

AOMS facilitate weight reduction that improves health by:

- Improving current complications such as T2DM, OSA, hypertension
- Preventing complications

Why would a PA choose to prescribe AOMS?

To facilitate weight reduction

To improve adherence to nutrition plans

To counter the effects of metabolic adaptation & prevent weight regain

After weight loss, metabolic adaptation occurs, which

- Increases hunger hormones
- Decreases satiety hormones
- Reduces resting metabolic rate

AOM Clinical Documentation

“The purpose of anti-obesity mediations is to treat the disease of obesity and facilitate the management of eating behavior, as well as slow the progression of weight gain and regain.

Pt has FDA indication for use with BMI>30 (BMI >27 and co-morbid conditions). Patient has failed lifestyle intervention with nutrition and physical activity changes and per AACE guidelines, pharmacotherapy is medically indicated.”

Given Stephen's health status, risk & history, would he benefit from AOMs?

Orlistat

Orlistat

- **Mechanism of action:** Blocks the digestion & absorption of fat in the stomach & intestines
- **Dosing:** 120 mg po TID Rx (60 mg po TID OTC)
- **DEA schedule:** V
- **Pregnancy:** X

Xenical (orlistat) prescribing information. South San Francisco, CA; Genentech USA, Inc.; 2016.

Orlistat (cont.)

- **Drug interactions:** Decreases fat-soluble agent absorption—vitamins A,D, E, K—warfarin, levothyroxine, metformin, antiepileptics, antiretrovirals

- **Most common adverse effects:** Oily stool & spotting, gas & anal leaking, bowel urgency & incontinence

- **Contraindications:** Chronic malabsorption syndrome, cholestasis, pregnancy

Orlistat

Brand name: Xenical (Rx); Alli (OTC)

Each tablet is: 120 mg (Xenical); 60 mg (Alli)

Take 1 tablet TID with meals

Is orlistat an option for Stephen?

Clinical Pearls

Orlistat

- Use of this medication is predicated on the idea that fat intake is undesirable
- Use with low-fat diets (<30% fat)
- Increases risk of kidney stones

How would you educate Stephen about orlistat?

1. Take with meals or up to one hour after meal
2. Skip dose if the meal didn't contain fat
3. Educate him about decreased fat-soluble agent absorption & the timing of fat-soluble supplements /meds—take at least 2 hours before or 2 hours after taking medication
4. Thoroughly explain side effects
5. Encourage him to wear dark pants & carry a change of clothes

Phentermine-Topiramate XR

Phentermine-Topiramate XR

- **Mechanism of action:** Works in hypothalamus to suppress cravings & hunger & promote satiety
- **Dosing:** Starting dose is 3.75/23, titrate to 15 mg/92 mg
- **DEA schedule:** IV
- **Pregnancy:** X

Phentermine-Topiramate XR (cont.)

- **Drug interactions:** May potentiate CNS depressants, potential hypokalemia with non-potassium sparing diuretics

- **Most common adverse effects**: Insomnia, constipation, dry mouth, dizziness, lightheadedness, difficulty concentrating, paraesthesias

- **Contraindications:** Pregnancy or seeking pregnancy, nursing, glaucoma, uncontrolled hyperthyroidism, MAOI w/in past 14 days, allergy to either component

Qsymia (phentermine/topiramate) prescribing information. Mountain View, CA: Vivus, Inc.; 2014.

Phentermine-Topiramate XR

REMS program

- Counsel females of reproductive potential at initial & all follow-up visits on the increased risk of orofacial clefts in infants exposed to phentermine-topiramate during the first trimester of pregnancy
- Counsel females of reproductive potential to have a pregnancy test before starting phentermine-topiramate & monthly thereafter during therapy
- Discuss the need for consistent use of effective contraception during therapy

Phentermine / Topiramate XR

Brand name: Qsymia

Four strengths:

1. 3.75 mg/ 23 mg capsule
2. 7.5 mg / 46 mg capsule
3. 11.25 mg / 69 mg capsule
4. 15 mg / 92 mg capsule

Titration schedule :

Weeks 1-2: One 3.75/23 mg capsule q am

Weeks 3-12: One 7.5/46 mg capsule q am

If patient hasn't lost 3% of weight by week 12, discontinue or escalate to:

Weeks 13-14: One 11.25/69 mg capsule q am

Weeks 14-on: One 15/92 mg capsule q am

Is Phentermine-Topiramate XR an option for Stephen?

How would you educate Stephen about phentermine / topiramate?

1. If Stephen was Stephanie, you would review the REMS & insist on 2 forms of birth control
2. He may experience dry mouth, constipation, or insomnia
3. He may experience somnolence / brain fog
4. Don’t take too late in the day or it could disrupt sleep

Clinical Pearls

Phentermine-Topiramate XR

- Great for soda drinkers
- Tread lightly with patients w/high functioning work
- Clinical Documentation:

  “Pt has no contraindication for use. If pt is female of reproductive age, have reviewed REMS and d/w pt need for 2 forms of birth control. Reviewed SEs and titration schedule. Rx sent. All questions answered. F/U as scheduled.”

Mail order home delivery: $112

Naltrexone HCL / Bupropion HCL Extended Release

Naltrexone HCL / Bupropion HCL

- **Mechanism of action:** Targets appetite regulation and reward system in the brain to decrease hunger & food cravings
- **Dosing:** Initiate at 8 mg / 90 mg & titrate over four weeks to 4 tablets per day
- **DEA schedule:** V
- **Pregnancy:** X

Naltrexone HCL / Bupropion HCL (cont.)

- **Drug interactions:** Opioid analgesics, interaction with CYP2D6 metabolized medications, beware of meds that lower seizure threshold

- **Most common adverse effects**: Nausea, vomiting, dizziness, insomnia, constipation or diarrhea, headache, dry mouth, disgeusia

- **Contraindications:** Use within 14 days of MAO-I, uncontrolled HTN, seizure disorders, eating disorders, opioid use, pregnancy, breastfeeding, excess alcohol use

Contrave (naltrexone/bupropion) prescribing information. La Jolla, CA: OrexigenTherapeutics, Inc.; 2016.

Naltrexone HCL / Bupropion HCL

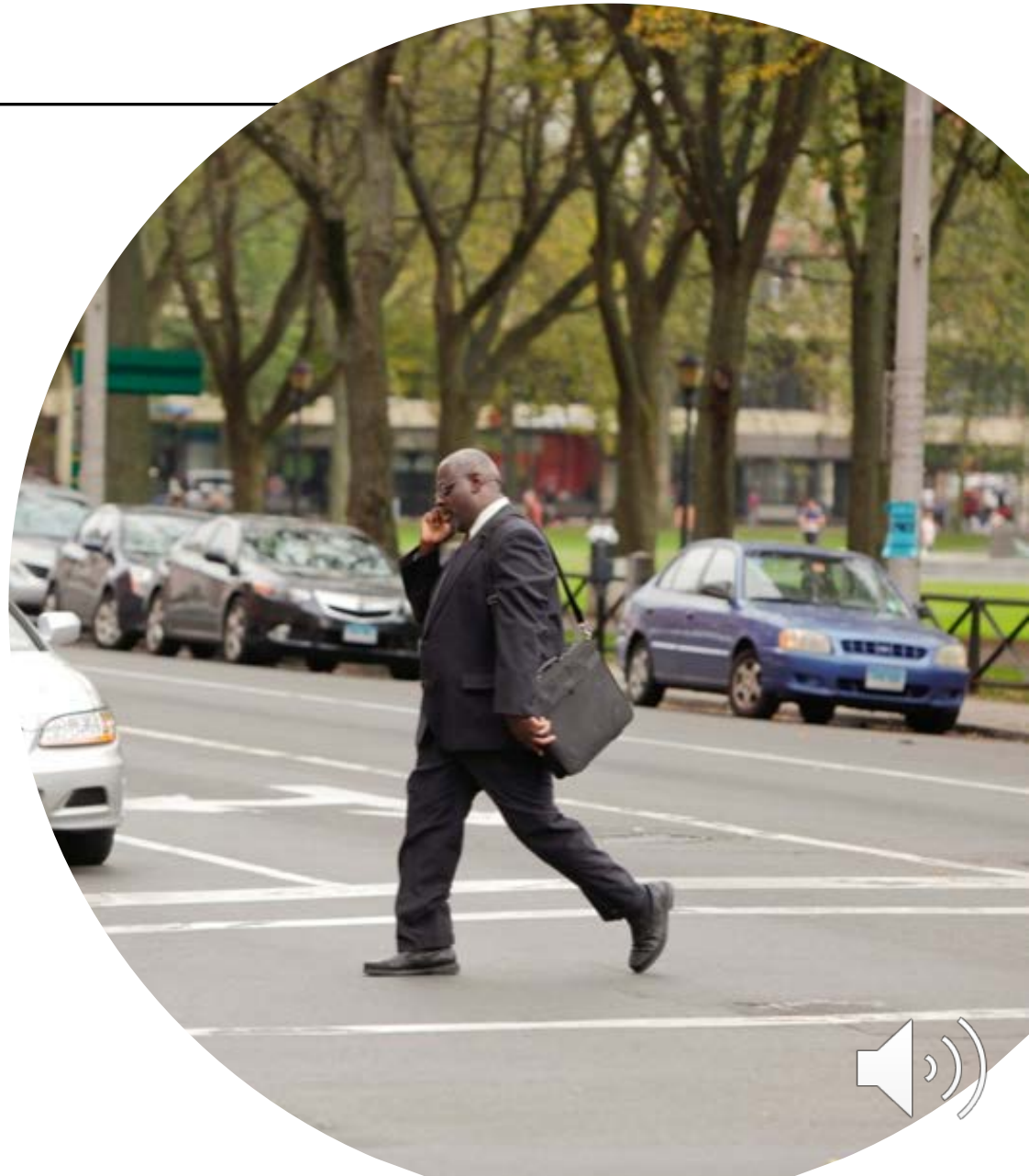
Brand name: Contrave

Each tablet is 8 mg/90 mg

Titration schedule is:

- Week 1: One tablet in a.m., no tablets in p.m.
- Week 2: One tablet in a.m., one tablet in p.m.
- Week 3: Two tablets in a.m., one tablet in p.m.
- Week 4 & beyond: Two tablets in a.m., two tablets in p.m.

Is naltrexone / bupropion an option for Stephen?



Clinical Pearls

Naltrexone / Bupropion

- Great for patients with cravings, emotional eating, and/or evening hunger
- Take with food to minimize nausea
- Although the label suggests weekly dose increases to achieve full dosing
  - Titrate based on patient's response & SE
  - Use the lowest dose to achieve desired results & manage SE
- Clinical documentation:

  "Start at one tablet in the morning x 1 week, increase to one twice a day week 2, increase to 2 in the AM, 1 in PM week three, and to 2 twice daily week 4 as tolerated. Pt has no hx of seizures, is not on narcotics. Side effects reviewed in detail. Stay well hydrated. All questions answered. "

If no AOM coverage, cash price is $99-119 per 120 tabl

How would you educate Stephen about naltrexone / bupropion?

1. Black box warning: suicidal thoughts & behaviors; neuropsychiatric reactions
2. Should not be taken with a high fat meal because of a resulting significant increase in bupropion & naltrexone systemic exposure
3. Reduced alcohol tolerance reported, so needs to be minimized

Liraglutide 3.0 mg

Liraglutide 3.0 mg

- **Mechanism of action:** Targets GLP-1 receptors in the brain to decrease hunger & increase satiety
- **Dosing:** Initiate at 0.6 mg per day SQ for one week; in weekly intervals, increase the dose until a dose of 3 mg is reached
- **DEA schedule:** V
- **Pregnancy:** X

Liraglutide 3.0 mg (cont.)

- **Drug interactions:** Delays gastric emptying, so may impact oral medications taken at the same time. Don't take with other GLP-1s

- **Most common adverse effects**: Nausea, vomiting, constipation, diarrhea, headache

- **Contraindications:** Personal or family history of medullary thyroid carcinoma or multiple endocrine neoplasia syndrome 2, pregnancy, breastfeeding

Saxenda (liraglutide injection) prescribing information. Plainsboro, NJ: Novo Nordisk Inc.; 2019

Liraglutide 3.0 mg

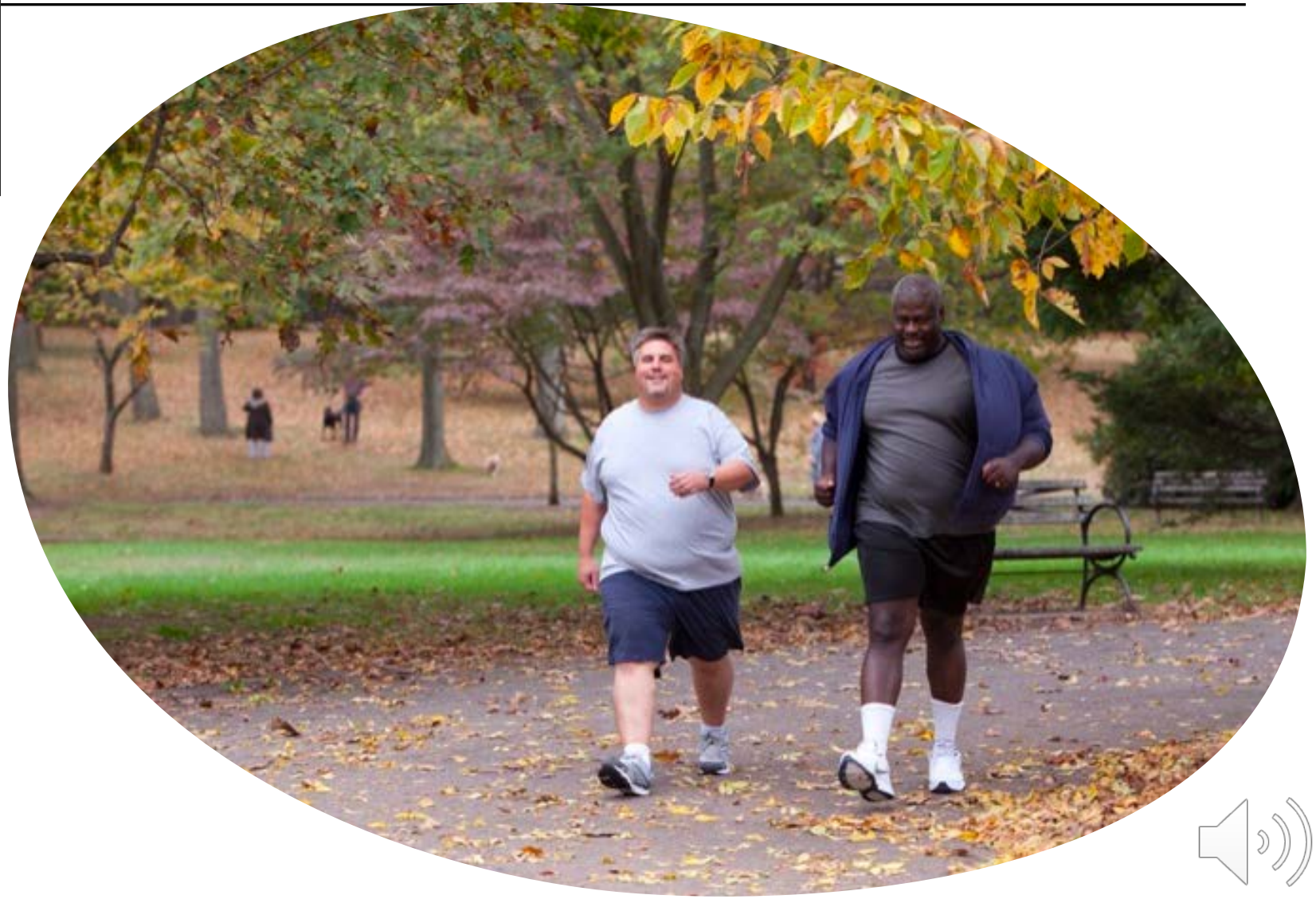
Brand name: Saxenda

- Medication supplied in multi-dose pens

Titration schedule:

- Week 1 = 0.6 mg once daily
- Week 2 = 1.2 mg once daily
- Week 3 = 1.8 mg once daily
- Week 4 = 2.4 mg once daily
- Week 5 = 3.0 mg once daily

Is Liraglutide 3.0 mg an option for Stephen?



Clinical Pearls

Liraglutide 3.0 mg

Although label suggests weekly dose increases to achieve full dosing

- Titrate based on patient's response & SE
- Use the lowest dose to achieve desired results & manage SE

Dose can be adjusted by "micro-clicks" if full dose increases cause significant SE. (This is off-label.)

- There are 10 "micro-clicks" per 0.6 mg
- Increase by 1-2 "micro-clicks" & monitor
- Once tolerated for 2-3 days, increase again

Clinical Documentation:

"Start at 0.6 mg sq daily & titrate up by 0.6 mg weekly as tolerated to max dose of 3 mg. If SE occur with dose increases, drop back to previous dose and increase by 2 small clicks every 2 days as tolerated. Pt has no hx, family or personal hx of MTC, MENS2. d/w pt potential SE including GI nausea, vomiting, change in bowel. instructed to stay well hydrated with 60 oz hydration intake daily. If left upper quadrant pain radiating to the back,w/w/o N/V, pt to [illegible] med and have labs drawn."

How would you educate Stephen about liraglutide 3.0 mg?

1. The needle is thinner than your eyelash
2. The most common side effects are nausea & constipation
3. Nausea is often resolved by eating a small snack or meal
4. Eat small portions due to slow gut motility—overeating can increase nausea / GERD
5. This medication provides benefits that are closest to those of bariatric surgery

Phentermine

Phentermine

- **Mechanism of action:** Works in hypothalamus to suppress cravings & hunger
- **Dosing:** 8–37.5 mg daily
- **DEA schedule:** IV
- **Pregnancy:** X

Phentermine (cont.)

- **Drug interactions:** Monoamine oxidase inhibitors, sympathomimetics, antidepressants, alcohol, adrenergic neuron blocking drugs, & some anesthetic agents

- **Most common adverse effects:** Dry mouth, constipation, restlessness, insomnia, headache

- **Contraindications:** CV diagnosis, uncontrolled HTN, hyperthyroidism, glaucoma, drug abuse history, MAO inhibitor in past 14 days, pregnancy, nursing

Adipex-P prescribing information. Sellersville, PA: Teva Pharmaceuticals.; 2013

Phentermine

Brand name: Lomaira (8 mg), Adipex

- 8 mg tablets (Lomaira)
- 15 mg or 30 mg capsule
- 37.5 mg tablet or capsule

Dosing options:

- Lomaira 8mg—1 tablet TID
- 15 mg capsule: 1 capsule once daily to BID
- 37.5 mg tablet: ½ tablet once daily to BID

Maximum dose is 37.5 mg daily

Phentermine

****Follow the prescribing laws in your state****

FDA approved for short-term use, but frequently prescribed off-label for long-term use

Package insert states potential for addiction, but there are no withdrawal symptoms

Thoughts about the Long-Term Use of Phentermine

Obesity is a chronic, progressive, disease such that intermittent/short term therapy is not medically appropriate

Phentermine / topiramate (Qsymia) is FDA approved for chronic use with phentermine 15mg as a component

“There currently is minimal evidence of any serious long-term side effects when phentermine is used alone for weight control.”

The Journal of Clinical Endocrinology & Metabolism, Volume 100, Issue 5, 1 May 2015, Pages 2135–2136,https://doi.org/10.1210/jc.2015-1782

Endocrine Society Position on the Long-Term Use of Phentermine

"Given the wide clinical prescribing of phentermine for more than 20 years and the lack of evidence of serious side effects, even in the absence of long-term controlled safety and efficacy data, it seems reasonable for clinicians to prescribe phentermine long term as long as the patient:

- Has no evidence of serious CVD
- Does not have serious psychiatric disease or a history of substance abuse
- Has been informed about weight loss medications that are FDA approved for long-term use and told that these have been documented to be safe and effective whereas phentermine has not
- Does not demonstrate a clinically significant increase in pulse or BP when taking phentermine
- Demonstrates a significant weight loss while using this medication"

Apovian, CM, Aronne, LJ, Bessesen, DH, et al. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2015; 100: 342-362

Obesity Medicine Association Position on the Long-Term Use of Phentermine

"The use of phentermine for longer than 12 weeks is supported by data and opinion leaders."

Bays, H.E., McCarthy, W., Christensen, S., Tondt, J., Karjoo, S., Davisson, L., Ng, J., Golden, A., Burridge, K., Conroy, R., Wells, S., Umashanker, D., Afreen, S., DeJesus, R., Salter, D., Shah, N. (2020). Obesity Algorithm eBook, presented by the Obesity Medicine Association. https://obesitymedicine.org/obesity-algorithm/

Is phentermine an option for Stephen?

Clinical Pearls

Phentermine

- Start at 7-9 am to determine response—onset, duration, side effects (particularly insomnia)
- Gradually shift timing by one hour until you find the time that provides evening coverage (if desired) without disrupting sleep
- Clinical Documentation:

  "Pt aware of FDA approval for short term therapy of 3 months, though evidence-based data shows success and safety with long term treatment. Pt has no unstable CV disease; BP is well controlled. No chance of pregnancy, pregnancy prevention reviewed. Timing of medication and SEs d/w pt. in detail. All questions answered."

8 mg (Lomaira) available for $30-50 for 60/90 tablets with GoodRx

How would you educate Stephen about phentermine?

1. If SE occur, they will peak in the first few days and typically resolve in 1-2 weeks
2. He may experience dry mouth, constipation, or insomnia
3. Don’t take too late in the day or it may disrupt sleep

How long should Stephen continue an AOM?

AOM continuation & discontinuation

If favorable response and no safety issues, continue medication

If no clinical improvements after 12-16 weeks, increase dose or switch to another med

If patient hasn't achieved 5% weight loss at 3 months, Endocrine Society recommends discontinuing and considering another medication*

*Specific label recommendations:

Contrave: D/C if hasn't lost 5% after 12 weeks on maintenance dose

Saxenda: D/C if hasn't lost 4% after 16 weeks of 3.0 mg

Qsymia: D/C if hasn't lost 5% after 12 weeks at highest dose

Let’s revisit the purposes of AOMs…

Treat	Facilitate	Slow	Improve
Treat the disease of obesity	Facilitate the management of eating behavior	Slow the progression of weight gain & regain	Improve weight, health, & quality of life

Bays, H.E., McCarthy, W., Christensen, S., Tondt, J., Karjoo, S., Davisson, L., Ng, J., Golden, A., Burridge, K., Conroy, R., Wells, S., Umashanker, D., Afreen, S., DeJesus, R., Salter, D., Shah, N. (2020). Obesity Algorithm eBook, presented by the Obesity Medicine Association. https://obesitymedicine.org/obesity-algorithm/

Clinical Pearls

Continuation vs. Discontinuation

- The guidelines haven’t caught up with the fact that obesity is a chronic disease & treatment goals go beyond weight loss

- Before discontinuing an AOM, consider the goals of:
    - Maintaining weight loss
    - Preventing further weight gain
    - Improvement of other conditions
    - Quality of life

Obesity management is chronic disease management

Pharmacotherapy may need to be continued indefinitely

This is **exactly** how we treat other chronic diseases such as diabetes & hypertension

Apovian, et al., 2015), (Eckel, Bays, Klein, &, Horn, 2015. Eckel, Bays, Klein, &, Horn, 2015.

What we've learned…

Obesity is a chronic, progressive, relapsing disease that requires comprehensive long-term treatment

AOMs are evidence-based tools that facilitate weight reduction, which improves health & quality of life

Resources for AOM Knowledge:

AACE Obesity Resource Toolkit	• http://obesity.aace.com/obesity-resource-toolkit
OMA Algorithm	• https://obesitymedicine.org/obesity-algorithm/download-now/
Obesity Medicine Association Infographics	• Online Store @ https://obesitymedicine.org/
The Obesity Patient Pages	• http://tosconnect.obesity.org/obesity/publications/obesity-journal/patient-pages

References

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