Overview of Pharmacotherapy for Chronic Weight Management

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Obesity

- Chronic and progressive metabolic condition stemming from a myriad of factors including genetic, physiological, environmental

Diagnosis of Obesity

- Evaluation of medical history, physical exam, labs, review of systems, medications
- Weight, BMI, and waist circumference
- Cardiometabolic disease risk

Comprehensive treatment

- Lifestyle interventions for all: healthy meal plans, physical activity, health education
- Medications for weight loss
- Weight loss devices
- Other surgical procedures

Pharmacotherapy Considerations

- BMI ≥ 30 or BMI ≥ 27 kg/m^2 with ≥ 2 comorbidities
- Comorbidities, cardiometabolic disease risk
- Contraindications and precautions
- Patient preference
- Cost

Phentermine-topiramate (Qysmia®) - C-IV

Dosage form and dosing:
- ER capsule, approved in patients ≥ 12 years of age
- Initiate at 3.75 mg/23 mg once daily for 14 days then increase to the next dose every 14 days. Max dose: 15 mg/92 mg once daily.

Mechanism:
- Phentermine stimulates release of norepinephrine which increases anorexigenic signaling
- Topiramate decreases orexigenic signaling and increases anorexigenic signaling

Weight loss compared to placebo:
6.6-8.6 kg (1 year)

Side effects:
Constipation, dry mouth, paresthesia, insomnia

Clinical pearls:
- Titrate slowly, avoid max doses if depression and anxiety
- Contraindicated in those with recurrent kidney stones, glaucoma, hyperthyroidism, and MAOI use
- Requires monitoring of HR, BP, BG, Scr, electrolytes, and new or worsening depression
- D/c if ≥ 5% reduction not achieved after 12 weeks

Semaglutide (Wegovy®) / Liraglutide (Saxenda®)

Dosage form and dosing:

Semaglutide (Wegovy®)
- Subcutaneous injection pen
- Initiate at 0.25 mg SC once weekly for 4 weeks. In 4 week intervals, increase the dose until a maintenance dose of 2.4 mg is reached.

Liraglutide (Saxenda®)
- Subcutaneous injection pen
- Initiate at 0.6 mg SC daily for 1 week. In weekly intervals, increase the dose until a dose of 3 mg is reached.
- Approved for ≥ 12 years of age

Mechanism:
- Stimulation of GLP-1 receptors in the hypothalamus decreases orexigenic signaling
- Lowers body weight through decreased calorie intake

Weight loss compared to placebo:
Semaglutide (Wegovy®): 12 kg (1 year)
Liraglutide (Saxenda®): 5.8 kg (1 year)

Side effects:
Nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distention, eructation, hypoglycemia in patients with type 2 diabetes, flatulence, gastroenteritis, and gastroesophageal reflux disease

Clinical pearls:
- Contraindicated in those with c-cell thyroid cancer
- When used in patients with type 2 diabetes - monitor BG; change in antihyperglycemics maybe required
- Monitor for HR, renal function, signs/symptoms of pancreatitis and worsening depression or suicidal ideation
- Discontinue Saxenda® if at least 4% weight loss not achieved by week 16
- Wegovy® may impact the absorption of concomitantly administered oral medications

Setmelanotide (Imcivree®)

Dosage form and dosing:
- Subcutaneous injection vial
- ≥ 12 years: 2 mg daily for 2 weeks, increase to 3 mg SC daily
- 6-12 years: 1 mg SC daily for 2 weeks, increase to 2 mg SC daily

Mechanism:
Stimulates melanocortin 4 receptors in brain

Weight loss compared to placebo:
14-28 kg (1 year)

Side effects:
Skin hyperpigmentation, injection site reactions, nausea, diarrhea, abdominal pain, vomiting, headache, fatigue, depression, and spontaneous penile erection

Clinical pearls:
- Approved in patients 6 years and older with POMC, PCSK1, or LEPR genetic deficiency or Bardet-Biedl syndrome (BBS)
- Discontinue if ≥ 5% reduction in baseline weight or BMI not achieved after 12 to 16 weeks

Phentermine (Adipex-P®, Lomaira®) - C-IV

Dosage form and dosing:
- Capsule and tablet
- Adipex-P®: 15-37.5 mg daily before breakfast or 1-2 hours after breakfast
- Lomaira®: 8 mg three times a day 30 minutes before a meal

Mechanism:
Stimulates the release of norepinephrine which leads to more energy expenditure and appetite suppression

Weight loss compared to placebo:
3.6 kg (2-24 weeks)

Side effects:
Hypertension, tachycardia, dry mouth, dizziness, irritability, insomnia, constipation, anxiety

Clinical pearls:
- Contraindicated in those with anxiety, drug use disorder, CV disease, hyperthyroidism, and glaucoma
- Approved for short-term (≤12 weeks) use only

Naltrexone-bupropion (Contrave®)

Dosage form and dosing:
- ER tablet
- Initiate at 8 mg/90 mg once daily for 1 week then 1 tablet twice daily for 1 week, then adding 1 additional tablet every week until 2 tablets twice daily. Max dose: 32 mg/360 mg per day.

Mechanism:
- Naltrexone - opioid antagonist
- Bupropion - weak inhibitor of dopamine and norepinephrine reuptake
- Decreased orexigenic signaling leading to decreased food intake

Weight loss compared to placebo:
4.9 kg (1 year)

Side effects:
Constipation, nausea, vomiting, headache, dizziness

Clinical pearls:
- Contraindicated in acute opiate withdrawal, bulimia or anorexia nervosa, concomitant use of chronic opioids, seizure disorder or past history of seizures, uncontrolled hypertension
- Discontinue if ≥ 4-5% reduction not achieved after 12 weeks at maintenance dose (15 weeks of treatment total)
- Monitor for BP, HR, BG, renal function in elderly patients, and new or worsening neuropsychiatric conditions

Orlistat (Xenical®, Alli® - OTC)

Dosage form and dosing:
- Capsule
- 60 or 120 mg three times daily with meals containing fat (during or up to 1 hr)

Mechanism:
Blocks absorption of dietary fats

Weight loss compared to placebo:
2.9-3.4 kg (1 year)

Side effects:
Oily spotting and evacuation, fecal urgency, fecal incontinence, increased defecation, flatus with discharge

Clinical pearls:
- Contraindicated in those with chronic malabsorption syndrome, cholestasis, and oxalate kidney stones
- Fiber supplement can assist with GI ADRs
- Supplement patient with fat-soluble vitamins 2 hrs before or after

References: 1) Garvey et al. AACE/ACE Obesity Clinical Practice Guidelines. Endocrine Practice. 2016;22(3):1-203. 2) Package inserts of Qysmia®, Wegovy®, Saxenda®, Imcivree®, Adipex-P®, Lomaira®, Contrave®, Xenical®, and Alli®