Weight Management Through Pharmacotherapy

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Concurrent Medications
**Identify and manage concomitant pharmacotherapy that might alter body weight**

**Cardiovascular medications**
- May increase body weight
  - Some beta-blockers
    - Propranolol
    - Atenolol
    - Metoprolol
  - Dihydropyridine (“dipine”) calcium channel blockers
    - Nifedipine
    - Amlodipine
    - Felodipine

**Diabetes mellitus medications**
- May increase body weight
  - Most insulins
  - Sulfonylureas
  - Thiazolidinediones
  - Meglitinides
  - May decrease body weight
    - Metformin
    - Glucagon-like peptide-1 agonists
    - Sodium glucose co-transporter 2 inhibitors
    - Alpha glucosidase inhibitors

**Metformin**
- May help improve adiposopathic disorders such as:
  - Insulin resistance
  - Polycystic ovarian syndrome
  - Fatty liver
  - Cardiovascular disease (especially when compared to sulfonylurea)
- May help treat complications of other concurrent drug treatments:
  - Antipsychotic-related weight gain
  - Human immunodeficiency virus protease inhibitor-associated abnormalities such as HIV lipodystrophy
- May help reduce the overall cancer rate, and help improve the treatment of multiple cancers:
  - Colon
  - Ovary
  - Lung
  - Breast
  - Prostate

References: [7]: [18]: [57]: [69]
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Identify and manage concomitant pharmacotherapy that might alter body weight

**Hormones**
- May increase body weight
  - Glucocorticoids
  - Estrogens
- May decrease body weight
  - Progestins
  - Testosterone

**Anti-seizure medications**
- May increase body weight
  - Carbamazepine
  - Gabapentin
  - Valproate
- May decrease body weight
  - Lamotrigine
  - Topiramate
  - Zonisamide

Identify and manage concomitant pharmacotherapy that might alter body weight

**Antidepressants**
- Generally increase body weight
  - Some tricyclic antidepressants ( tertiary amines)
    - Amitriptyline
    - Desipramine
    - Imipramine
    - Some selective serotonin reuptake inhibitors (e.g. paroxetine)
    - Some irreversible monoamine oxidase inhibitors
    - Bupropion
    - Mirtazapine
- Generally decreases body weight
- Variable effects on body weight
  - Some tricyclic antidepressants ( secondary amines)
    - Desipramine
    - Nortriptyline
    - Protriptyline
    - Some selective serotonin reuptake inhibitors
    - Citalopram
    - Escitalopram
    - Fluoxetine
    - Sertraline
    - Some serotonin and norepinephrine reuptake inhibitors
    - Desvenlafaxine
    - Duloxetine
    - Venlafaxine
    - Some irreversible monoamine oxidase inhibitors (e.g. tranylcypromine)
Identify and manage concomitant pharmacotherapy that might alter body weight

**Mood Stabilizers**

- May increase body weight
  - Gabapentin
  - Lithium
  - Valproate
  - Vigabatrin
  - Variable or neutral effects upon body weight
  - Carbamazepine (sometimes reported to increase body weight)
  - Lamotrigine (sometimes reported to decrease body weight)
  - Oxcarbazepine

**Migraine Medications**

- May increase body weight
  - Amitriptyline
  - Gabapentin
  - Paroxetine
  - Valproic acid
  - Some beta-blockers
  - May decrease body weight
  - Topiramate

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Identify and manage concomitant pharmacotherapy that might alter body weight

**Antipsychotics**

- May substantially increase body weight
  - Clozapine
  - Olanzapine
  - Zotepine
  - May somewhat increase body weight
  - Aripiprazole
  - Chlorpromazine
  - Iloperidone
  - Paliperidone
  - Quetiapine
  - Risperidone
  - Sertindole
  - Lithium
  - May have limited effects on body weight
  - Benzodiazepines
  - Multimodal hypnotherapy
  - Trizodone

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Reference/s: [18] [57] [73] [74] [75] [76]
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**Treatment**

**Identify and manage concomitant pharmacotherapy that might alter body weight**

- Human Immunodeficiency Virus (HIV) medications
- Chemotherapies

- May increase body weight:
  - Some highly active antiretroviral therapies (HAART) protease inhibitors without HIV lipodystrophy
- May decrease body weight:
  - Some highly active antiretroviral therapies (HAART) protease inhibitors with HIV lipodystrophy

- May increase body weight:
  - Tamoxifen
  - Cyclophosphamide
  - Methotrexate
  - 5-fluorouracil
  - Aromatase inhibitors
  - Corticosteroids

**Weight Management Pharmacotherapy**

Adjunct to nutritional, physical activity, and behavioral therapies

Objectives:
- Treat disease
- Adiposopathy or sick fat disease (SFD)
- Fat mass disease (FMD)
- Facilitate management of eating behavior
- Slow progression of weight gain / regain
- Improve the health, quality of life, and body weight of the patient with overweight or obesity

References: [18] [57] [73] [74] [75]

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Bays HE. Adiposopathy, diabetes mellitus, and primary prevention of atherosclerotic coronary heart disease: treating "sick fat" through improving fat function with antidiabetes therapies. Am J Cardiol 2012;110:4B-12B.
**Treatment**

**Pharmacotherapy**

- **Examples of weight management agents approved 1999 or before**
  - Phentermine
  - Diethylpropion
  - Phendimetrazine
  - Benzphetamine
  - Orlistat

- **Examples of weight management agents approved 2012 and beyond**
  - Lorcaserin
  - Phentermine HCl / topiramate extended-release
  - Naltrexone HCl / bupropion HCl extended-release
  - Liraglutide

**Sympathomimetic amines**

- Examples: Phentermine, diethylpropion, phendimetrazine, benzphetamine
- Increases satiety
- Drug Enforcement Agency Schedule weight management agents
- DEA IV for phentermine and diethylpropion
- DEA III for phendimetrazine and benzphetamine
- Potential adverse experiences include palpitation, tachycardia, increased blood pressure, overstimulation, tremor, dizziness, insomnia, dysphoria, headache, dryness of mouth, dysgeusia, diarrhea, constipation
- Pregnancy category X

**Gastrointestinal lipase inhibitors**

- Example: Orlistat
- Impairs gastrointestinal energy absorption
- Potential adverse experiences include oily discharge from the rectum, flatus with discharge, increased defecation, fecal incontinence, may increase risk of cholelithiasis, may increase risk of urinary oxalate, rare postmarketing reports of severe liver injury, may decrease fat-soluble vitamin absorption (e.g., vitamins A, D, E, K, and beta carotene)
- Pregnancy category X

Reference(s): [500] [502]
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Pharmacotherapy Treatment of Obesity

Food and Drug Administration (FDA) Principles

- FDA approved weight management pharmacotherapy indications:
  - Patients with obesity (e.g. BMI ≥ 30 kg/m²)
  - Patients who are overweight (e.g. BMI 27 kg/m²) with presence of increased adiposity complications (e.g. type 2 diabetes mellitus, hypertension, dyslipidemia)

- If no clinical improvement after 12 weeks with one weight management pharmacotherapy, then consider alternative weight management pharmacotherapy, or increasing weight management pharmacotherapy dose (if applicable).

*While BMI (body mass index) is the only measure listed in the prescribing information for weight management pharmacotherapy, BMI has limitations. Especially in muscular individuals or those with sarcopenia, overweight and obesity are more accurately assessed by other measures.

Lorcaserin

- Indications & use
  - Serotonin (5-hydroxytryptamine) 2c receptor agonist
  - Drug Enforcement Agency Schedule IV drug
  - Dose = 10 mg twice a day

- Potential drug interactions
  - The safety of lorcaserin coadministration with other serotonergic or antidopaminergic agents is not yet established, which includes selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, monoamine oxidase inhibitors, triptans, bupropion, dextromethorphan, St. John’s Wort

- Pharmacokinetics
  - Lorcaserin is metabolized in the liver with metabolites excreted in the urine.
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