Medications Used for Managing Obesity and Effect on Surgical Patients

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Objective

Discuss the epidemiology of obesity

Identify medication induced causes of obesity

Review the medication options available and effect on patients undergoing surgical procedures

Guidelines

American Diabetes Association (ADA): Standards of care in diabetes (2023)

Obesity and weight management for the prevention and treatment of type 2 diabetes

American Gastroenterological Association (AGA): Guideline on pharmacological interventions for adults with obesity (2022)

American College of Obstetricians and Gynecologists (ACOG): Practice bulletin on obesity in pregnancy(2021) AGA:

Clinical practice guidelines on intragastric balloons in the management of obesity(2021)

American Society of Clinical Oncology (ASCO): Appropriate systemic therapy dosing for obese adult patients with cancer (2021)

ACOG: Committee opinion on gynecologic surgery in the obese woman (2015, reaffirmed 2020)

ACOG: Committee opinion on physical activity and exercise during pregnancy and the postpartum period (2020)

Department of Veteran Affairs (VA)/Department of Defense (DoD): Clinical practice guideline for management of adult overweight and obesity (OBE) (2020)

Guidelines

ACOG: Committee opinion on ethical considerations for the care of patients with obesity (2019)

The Obesity Society (TOS): Position statement on obesity as a disease (2019)

American Heart Association (AHA): Science advisory on dietary diversity – Implications for obesity prevention in adult populations (2018)

USPSTF: Final recommendation statement on weight loss to prevent obesity-related morbidity and mortality in adults – Behavioral interventions (2018)

AHA: Scientific statement on meal timing and frequency: implications for cardiovascular disease prevention (2017)

Academy of Nutrition and Dietetics (AND): Position on interventions for the treatment of overweight and obesity in adults (2016)

AND: Position on obesity, reproduction, and pregnancy outcomes (2016)

American Association of Clinical Endocrinologists (AACE) and American College of Endocrinology (ACE): Comprehensive clinical practice guidelines for medical care of patients with obesity (2016)

Guidelines

AHA: Science advisory on sedentary behavior and cardiovascular morbidity and mortality(2016)

AHA: Scientific statement on identification of obesity and cardiovascular risk in ethnically and racially diverse populations (2015)

American Society for Reproductive Medicine (ASRM): Obesity and reproduction – A committee opinion (2015)

AACE/ACE and TOS: Clinical practice guidelines for healthy eating for the prevention and treatment of metabolic and endocrine diseases in adults (2013)

AHA/American College of Cardiology (ACC)/TOS: Guideline for the management of overweight and obesity in adults (2013)

American Society for Nutrition (ASN): Scientific statement on consumption of cereal fiber, mixtures of whole grains and bran, and whole grains and risk reduction in type 2 diabetes, obesity, and cardiovascular disease (2013)

American Society for Parenteral and Enteral Nutrition (ASPEN): Clinical guidelines on nutrition support of hospitalized adult patients with obesity (2013)

US Preventive Services Task Force (USPSTF): Final recommendation statement on healthy diet and physical activity for cardiovascular disease prevention in adults with cardiovascular risk factors – Behavioral counseling interventions (2020)

Guidelines

ASN: Consensus statement on energy balance and its components – Implications for body weight regulation (2012)

AHA: Scientific statement on assessing adiposity (2011)

AHA: Science advisory on cardiovascular evaluation and management of severely obese patients undergoing surgery (2009)

AHA: Science advisory on mortality, health outcomes, and body mass index in the overweight range (2009)

American College of Sports Medicine (ACSM): Position stand on appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults (2009)

Androgen Excess and Polycystic Ovary Syndrome Society (AE-PCOS): Position statement for the treatment of obesity in polycystic ovary syndrome (2009)

AHA: Scientific statement on population-based prevention of obesity – The need for comprehensive promotion of healthful eating, physical activity, and energy balance (2008)

AHA: Scientific statement on the contributory risk and management of comorbidities of hypertension, obesity, diabetes mellitus, hyperlipidemia, and metabolic syndrome in chronic heart failure (2016)

Definition of Obesity

WHO: “excess or abnormal fat accumulation that presents a risk to health”

CDC: “weight that is considered higher than what is considered healthy for a given height is described as overweight or obesity”

Both use BMI to further define:

- BMI: 25 to 29.9 kg/m^2 considered overweight
- BMI: ≥30 kg/m^2 as obesity
  - Class I: 30-34.9kg/m^2
  - Class II: 35-39.9 kg/m^2
  - Class III: ≥40 kg/m^2 (also referred to as severe, extreme, or massive obesity)

Epidemiology (U.S.)

Prevalence: 41.9% (March 2020)

- Increase from 30.5% in 1999
- Severe obesity increased to 9.2% (From 4.7% in 1999)

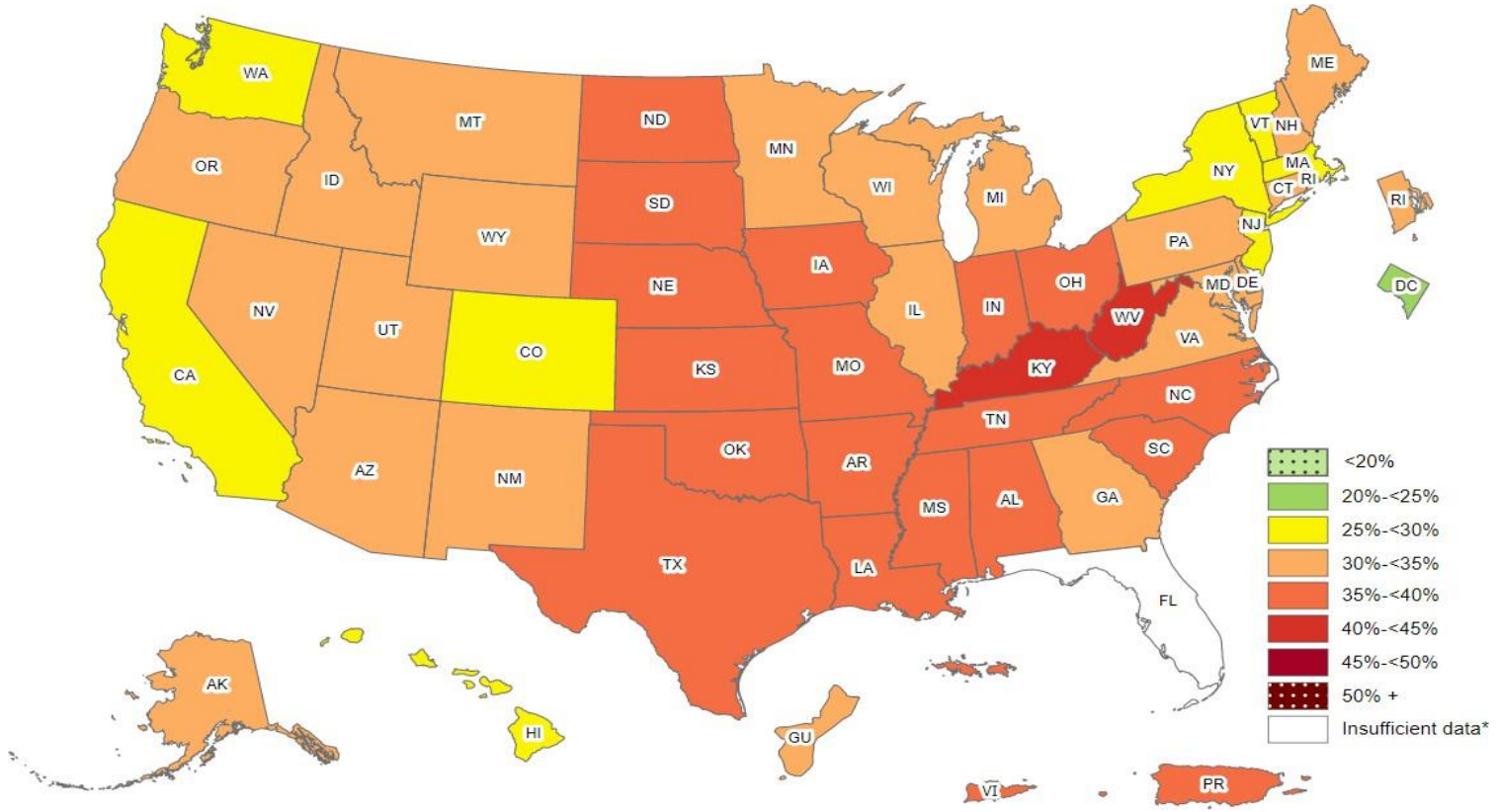
Incidence: equal in males and females

Estimated cost: $173 billion in 2019

Highest rates of obesity

- Non-Hispanic black adults: 49.9%
- Hispanic adults: 45.6%
- Non-Hispanic white adults: 41.4%
- Non-Hispanic Asian adults: 16.1%
- **Veterans: 78% (up from 64% in 1996)**

Adults Obesity Maps



Consequences of Obesity

Increase rate of chronic health conditions

- DM, HTN, metabolic syndrome, OSA, osteoarthritis, dyslipidemia, non-alcoholic fatty liver disease
- 23% of obese patients have DM
- 58% of obese patients have HTN

Reduced quality of life

- Perceive and experience stigma and discrimination with work, healthcare, and mass media
- Worsening of pain experience
- Worsening of psychosocial functioning

Increased healthcare expenditures

- Class III obesity incurred a 75% higher cost of medical expenditures than adults without obesity or being overweight
- Annual medical costs for adults with obesity were $1,861 higher per person than adults with healthy weight
- Severe obesity costs were $3,097 per person

Medication Causes of Obesity

Medication Class	Medications with potential weight gain
Antipsychotics	Quetiapine Clozapine Olanzapine Risperidone Thioridazine
Antidepressants	Mirtazapine TCAs MAOIs SSRIs (Paroxetine)
Antiepileptic/Mood stabilizers	Gabapentin Pregabalin Carbamazepine Divalproex Lithium Vigabatrin
Antihyperglycemic agents	Insulin Sulfonylureas Meglitinide analogs Thiazolidinediones
Beta Blockers	Metoprolol Atenolol Propranolol
Alpha blockers	Terazosin
Glucocorticoids	Prednisone Methylprednisolone Hydrocortisone
Hormonal Agents	Medroxyprogesterone Megestrol
Antihistamines	Cetirizine Cyproheptadine

History of Obesity Treatment

Health effects of obesity noted by Hippocrates and Sushruta

- Earliest treatments: diet, exercise, emetics, cathartics
- Emetics: honey water, hellebore plants
- Cathartics: bindweed, donkey milk with honey, wild parsley, thyme

Recommendations unchanged until the 20th century

1933 –Dinitrophenol (DNP): 1st anti-obesity therapy

- 1st year of use, DNP was used by 100,000 individuals in the US alone

1945-1962: Drug companies, produced amphetamine-based meds for tx of obesity as an adjunct to TLC

- 1944- desoxyephedrine (methamphetamine), manufactured by Endo Products
- 1946- the FDA questioned the wisdom of prescribing amphetamines for weight loss beyond its original purpose of treating narcolepsy, mild depression, hay fever, & chronic alcoholism, d/t the potential for addiction
- 1947-FDA confirmed the approval of the first version of desoxyephedrine from Endo Products, as well as a second version from Abbott Laboratories
- 1959- phentermine, developed by Strasenburgh Laboratories
  - At clinical doses, phentermine has a lower potential for addiction than other amphetamine-based therapies

History of Obesity Treatment (cont)

To reduce the addictive potential of the amphetamine-based anti-obesity drugs, analogues were developed

- 1956- phenmetrazine, was developed by Ciba Geigy Corp
- 1959- diethylpropion (Merrell National Drug) , benzphetamine (Upjohn) & phendimetrazine (Averst, McKenna & Harrison Ltd)

1950s- combined amphetamine analogues w/ a barbiturate

- Dextroamphetamine & amobarbital [Smith, Kline and French (now GlaxoSmithKline)
- Methamphetamine & pentobarbital (Abbott Laboratories)
- Methamphetamine & phenobarbital (Robin Pharmaceuticals Ltd)

1962: Kefauver–Harris amendment to the US Food, Drug & Cosmetic Act was passed in Congress

- Mandating the provision of substantial evidence of efficacy for all new drug applications (NDAs) , which includes those of obesity
- Obesity drugs approved prior to 1962 became subject to the 'Drug Efficacy Study' (DESI drug)
  - FDA called upon the National Research Council of the National Academy of Sciences to investigate efficacy & safety of previously approved drugs and categorize them as:
    - Effective
    - Effective but possibly efficacious, but other, more efficacious or safer drugs were available
    - Probably effective
    - Ineffective
    - Ineffective as a fixed combination

READ WHAT HAPPENED WHEN OBESE PATIENTS WERE SWITCHED from DESOXYN GRADUMET to a PLACEBO

THE CLINICAL STUDY*:

Twenty-five overweight patients, first on Desoxyn Gradumet, and then on a placebo.

THE RX:

A 1000-calorie diet and Desoxyn Gradumet, 10 or 15 mg., once a day for three months. Then an identically appearing placebo was substituted for Desoxyn Gradumet for the next three months.

THE CLINICAL RESULT:

During the first three months when they were on Desoxyn Gradumet, all of the patients lost weight, the average loss being 2.9 lbs. per week. During the next three months, when they were on a placebo, only three patients continued to lose weight, while three others started to gain weight. The remainder stayed at a status quo level.

3 Months Weight Loss on Desoxyn (lbs.)	3 Months Weight Loss on Placebo (lbs.)
Average 19 cases:	
26	0
6 individual cases whose weight changed in placebo period:	
13	2
15	2
40	5
20	5 (gained)
25	2 (gained)
20	5 (gained)

Side effects: The side effects were relatively insignificant except in two of the patients who experienced nervous discomfort.

A SIDELIGHT:

There was a noticeable reduction of obesity-induced lethargy and dyspnea. The investigator also noted that when the placebo was substituted for Desoxyn Gradumet, there was a loss of anorexia and a reversal of all effects.

THE CONCLUSION:

"Above all, in addition to the single daily dose form, the change in the obese patient's mental attitude, his added incentive not only to curb appetite but to pursue his daily occupation, was most favorable."

*McMahon, Thomas F., Private Communication to Medical Department, Abbott Laboratories, 1961.

THE DRUG:

DESOXYN® Gradumet®

All-Day Appetite Control from a Single Oral Dose—5, 10 or 15 mg.

Desoxyn Gradumet—Methamphetamine Hydrochloride in Long-Release Dose Form, Abbott. Gradumet—Long-release dose form, Abbott: U.S. Patent No. 2,987,445.

ABBOTT

'Amphedroxyn Hydrochloride'

(Methamphetamine Hydrochloride, Lilly)

IS OFTEN PREFERABLE TO OTHER FORMS OF AMPHETAMINE—

because—

smaller doses produce longer cerebral stimulation, with a minimum of undesirable excitement and other side-effects.

When patients with depression, narcolepsy, alcoholism, or obesity are selected as suitable cases for stimulant therapy, 'Amphedroxyn Hydrochloride' is a prudent choice of drug.

Lilly
SINCE 1876

Detailed information and literature on 'Amphedroxyn Hydrochloride' are personally supplied by your Lilly medical service representative or may be obtained by writing to Eli Lilly and Company, Indianapolis 6, Indiana, U.S.A.

Does more than curb appetite...
also relieves the tensions of dieting

new!

Appetrol

Helps you keep your patient on your diet

WALLACE LABORATORIES, New Brunswick, N. J.

Lady out of the Dark

The selective cerebral action of Norodin is useful in dispelling the shadows of mild mental depression. The reported advantages of Norodin over chemically related analepics include smaller dosages, more prompt and prolonged mental stimulation, and relatively few side effects. Norodin can be used to advantage in achieving the sense of well-being essential to effective patient management in functional and organic disturbances. In obesity, Norodin is useful in reducing the desire for food and counteracting the low spirits associated with the rigors of an enforced diet.

Supplied: 2.5 and 5 mg. tablets in bottles of 100

Norodin®

Hydrochloride

brand of methamphetamine hydrochloride

PSYCHOMOTOR STIMULANT AND ANTI-DEPRESSANT

Endo®

Endo Products Inc., Richmond Hill 18, N.Y.

"Either lose 45 pounds or wait for 6 more inches of snow!"

OBETROL®
for weight control

Each OBETROL-10 tablet contains: Methamphetamine Bacitharate 2.5 mg.; Methamphetamine Hydrochloride 2.5 mg.; Amphetamine Sulfate 2.5 mg.; Dextro-amphetamine Sulfate 2.5 mg.; (OBETROL-20 tablets contain twice this potency) Pat. #2746052.

This combination of amphetamines may be useful as an adjunct in the management of certain forms of obesity where an appetite depressant is indicated.

Contraindications: Hypertension, advanced arteriosclerosis, coronary artery disease, cardiac arrhythmias, peripheral vascular disease, states of motor restlessness, anxiety, excitement, agitated depression, hyperthyroidism, idiosyncrasy to amphetamine, concomitant administration of a monoamine oxidase inhibitor. **Precautions:** Use with caution in individuals with anorexia, insomnia, vasomotor instability, asthenia, psychopathic personality, a history of homicidal or suicidal tendencies, and individuals who are known to be hyperactive to sympathomimetic agents, or emotionally unstable individuals who are known to be susceptible to drug abuse. Certain monoamine oxidase inhibitors may potentiate the action of Obetrol. **Side Effects:** The most common side effects attended with the use of amphetamines include nervousness, irritability, euphoria, insomnia, dryness of mouth, nausea, vertigo, constipation, and headache.

Dosage and Administration: Initial adult dose is one-half to one Obetrol-10 tablet daily, preferably one-half to one hour before meals. This may be gradually increased to one Obetrol-10 or Obetrol-20 tablet one to three times daily as indicated. **Supplied:** Tablets scored, in bottles of 100, 500, and 1000.

REQUEST SAMPLES AND LITERATURE

OBETROL PHARMACEUTICALS • BROOKLYN, N.Y. 11207

DR._____

ADDRESS_____

CITY_____ STATE_____

SIGNATURE_____

OBETROL PHARMACEUTICALS
Div. of Rexar Pharmacal Corp., Brooklyn, N.Y. 11207

History of Obesity Treatment (cont)

1973-FDA approved marketing of 3 amphetamine-based meds for weight loss

- Fenfluramine (Robins Co.)
- Mazindol (Sandoz Pharmaceuticals)
- Chlorphentermine (Warner Chilcott)
- Safety concerns regarding the addictive potential of these drugs were never fully countered

1977- All approved amphetamine-derived anti-obesity drugs were restricted to short-term use (a few weeks)

1992-Combination of low-dose phentermine and fenfluramine (Fen-Phen) demonstrated average weight loss of 15.9% from baseline over 34 weeks with no major safety concerns during a follow-up period of up to 4 years' treatment (121 patients)

1996-Dexfenfluramine approved despite links to pulmonary HTN

1997-Restriction of dexfenfluramine & Fen-Phen use d/t left sided heart valve degeneration

2006-Rimonabant (CB1 receptor agonist) studied but never approved

Medication Classes for Obesity Treatment

Labeled for Obesity

- Stimulants
- GLP-1 agonists
- Antidepressant/opioid antagonist
- Lipase Inhibitor
- Carbonic anhydrase inhibitor/stimulant
- GIP/GLP1 Receptor Agonist

Unlabeled for Obesity

- Biguanide
- Carbonic anhydrase inhibitor
- SGLT-2 inhibitor
- Cyanocobalamin
- TRT
- Thyroid hormones

Stimulants (Phentermine, diethylpropion phendimetrazine, benzphetamine)

Name brand: Phentermine (Fastin, Adipex-P), no other name brands

- Diethylpropion & phendimetrazine still available depending on the state

Approval date: 1959: approved in Fen-Phen in the 1970s (removed from market in the 1990s)

MOA: Sympathomimetic amine w/ pharmacologic properties like amphetamines

- Reduces appetite secondary to CNS effects, including stimulation of the hypothalamus to release norepinephrine

Dose: 15 – 37.5mg po daily every morning (Dosing is presented in terms of the salt, phentermine hydrochloride (not as phentermine base))

- For short-term use (**up to 12 weeks**) as an adjunct to TLC in patients who cannot take preferred agents & who have a BMI ≥30 kg/m^2 **or** patients with a BMI ≥27 kg/m^2 and ≥1 weight-associated comorbidity (eg, dyslipidemia)

Stimulants (Phentermine, diethylpropion, phendimetrazine, benzphetamine)

Warnings

- Avoid in patients with heart disease, poorly controlled hypertension, pulmonary hypertension, or history of addiction or drug abuse

Contraindications

- Hypersensitivity or idiosyncrasy to phentermine, other sympathomimetic amines or any component of the formulation; history of cardiovascular disease (eg, arrhythmias, heart failure, coronary artery disease, stroke, uncontrolled hypertension); hyperthyroidism; glaucoma; agitated states; history of drug abuse; use during or within 14 days following MAO inhibitor therapy; pregnancy; breast-feeding

Pregnancy or breast feeding: NO

Cost: 15mg: $0.41/cap 37.5mg:$0.04/tab

Drug interactions:

- CNS stimulants, EtOH, TCA, MAOIs

Stimulants (Phentermine, diethylpropion, phendimetrazine, benzphetamine) Data

No long-term studies (at least 1 year)

All were approved before the necessity of long-term tx for obesity was established

None of the medications were required to meet the current efficacy benchmarks for weight loss relative to placebo

- ≥ 5% mean weight loss compared to placebo **OR**
- Proportion of drug-treated subjects who lose ≥ 5% of initial weight is ≥ 35%

Treatment duration limitation added in 1977 d/t abuse potential

- Continued issue with prescribers using off-label for longer periods of time

Meta-analysis of 108 studies showed that weight loss never exceed more that 4kg compared to placebo

All meds hampered by short duration, high attrition, small population

Stimulants Surgical Considerations

Malignant Hyperthermia

- Specifically, amphetamines but any stimulant can increase this risk

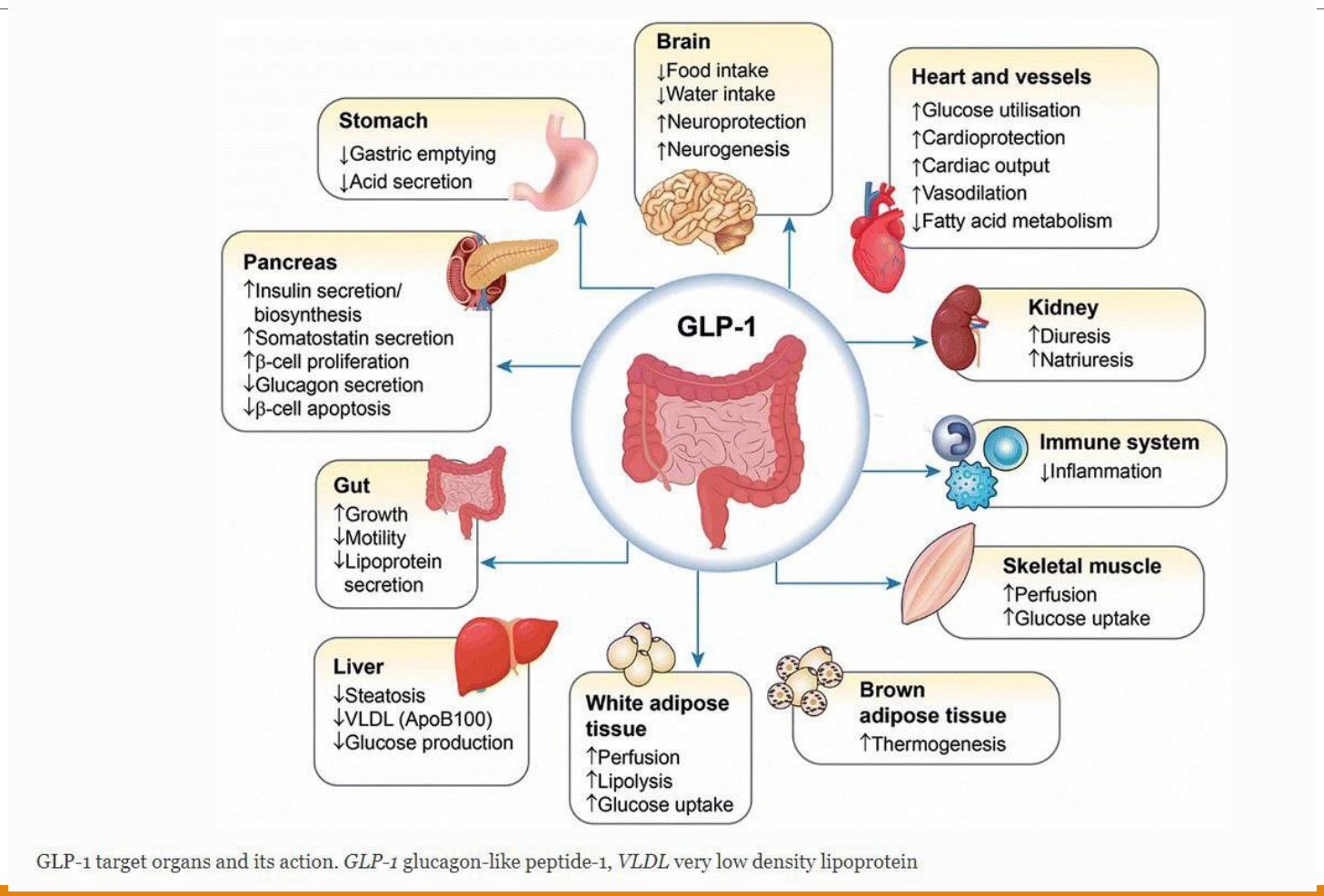
HTN post surgery

- Increased risk for post surgical complication

Mitigation Strategy

- Hold for 5 days prior to surgery
- Half life of med is 20 hours

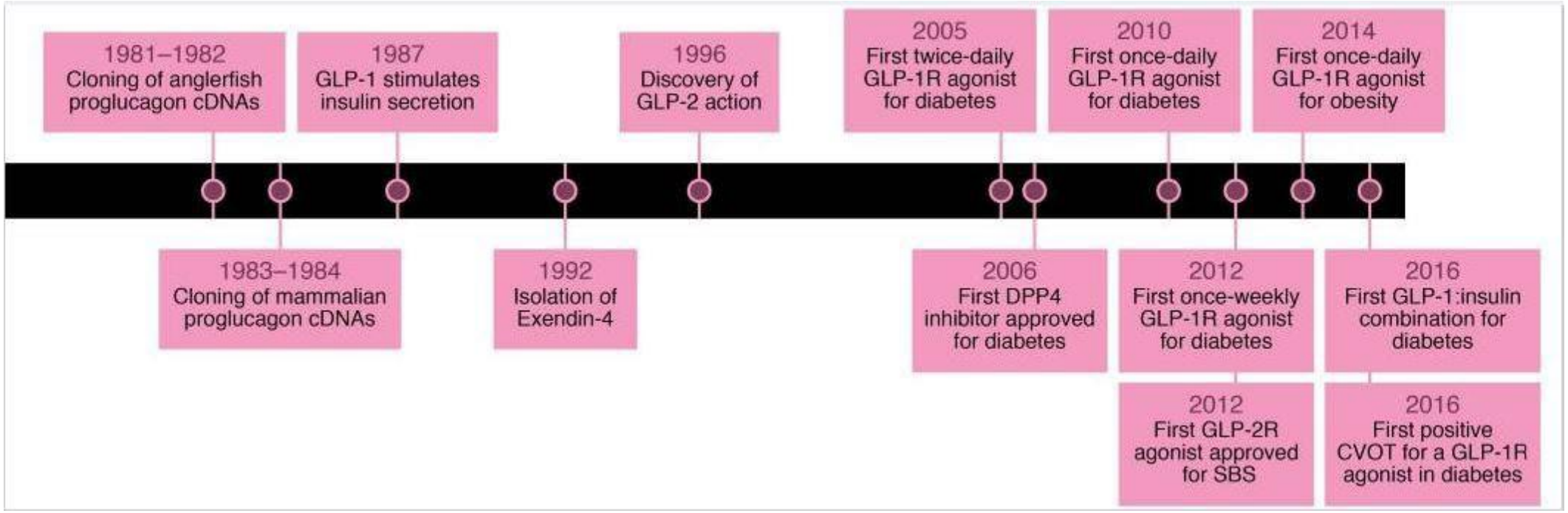
Glucagon-Like Peptide-1 (GLP-1)



GLP-1 target organs and its action. *GLP-1* glucagon-like peptide-1, *VLDL* very low density lipoprotein

Glucagon-Like Peptide-1 (GLP-1)

Glucagon-Like Peptide-1 (GLP-1)



GLP-1 Agonists

Weight loss	Diabetes
Saxenda (liraglutide)	Victoza (liraglutide)
Wegovy (semaglutide)	Ozempic (semaglutide)
Zepbound (tirzepatide)	Mounjaro (tirzepatide)
	Tanzeum (albiglutide) **
	Trulicity (dulaglutide)
	Rybelsus (oral semaglutide)
	Bydureon Bcise (Exenatide ER)
	Byetta (Exenatide)
	Adlyxin (Lixisenatide)*

*Discontinued 2/3/23
**Discontinued in 2017

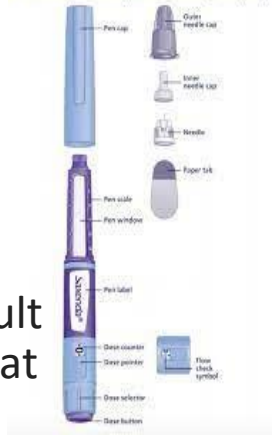
GLP-1 agonists (liraglutide)

Name brand: Saxenda®

FDA approval date: December 2014 (First approved GLP-1 agonist for weight loss)

Indications

- As an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index of ≥30 kg/m^2 (obesity) or ≥27 kg/m^2 (overweight) in the presence of at least 1 weight-related comorbid condition (e.g. HTN, type 2 DM, or dyslipidemia)



MOA: long-acting analog of human GLP-1 (an incretin hormone) which increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, increases B-cell growth/replication, slows gastric emptying, and decreases food intake

GLP-1 agonists (liraglutide)

Adult Dose

- Initial: 0.6 mg once daily for 1 week; increase by 0.6 mg daily weekly to a target dose of 3 mg/day
- Evaluate weight loss after 12 weeks; if at least **4%** of baseline body weight has not been lost, d/c use as continued treatment is not likely to be effective

Contraindications

- Patients with a personal or family history of medullary thyroid carcinoma (MTC)
- Patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN-2)
- Patients who are hypersensitive to liraglutide or to any ingredient in the formulation
- Women who are pregnant or breastfeeding

Cost

- 30 DS of 3mg daily = $543.50

GLP-1 agonists (liraglutide)

Warnings

- Thyroid C-cell Tumors
- Acute Pancreatitis
- Acute Gallbladder Disease
- Hypoglycemia
- Heart Rate Increase
- Renal Impairment
- Hypersensitivity Reactions
- Suicidal Behavior & Ideation

Adverse effects

- Nausea, diarrhea, constipation, vomiting, injection site reactions, headache, hypoglycemia, dyspepsia, fatigue, dizziness, abdominal pain, increased lipase, upper abdominal pain, pyrexia, and gastroenteritis

GLP-1 agonists (liraglutide)

Data

- SCALE (Satiety and Clinical Adiposity–Liraglutide Evidence in Nondiabetic and Diabetic people)
- Study 1
  - 56-week, randomized, double-blind, placebo-controlled study
  - Adult patients with a BMI of ≥30 kg/m^2 OR ≥27 kg/m^2 with 1 or more weight-related comorbidities (N=3,731) were randomized to receive once-daily liraglutide (n=2,487) or placebo (n=1,244) in conjunction with a TLC program that included increased physical activity and a 500-kcal/day deficit diet
  - Mean baseline weight: 106.2kg ± 21.2 for liraglutide & 106.2kg ± 21.7 for placebo
  - Avg weight loss from baseline: liraglutide 7.4% vs 3% placebo
  - % of participants losing ≥ 5% body weight: liraglutide 62.3% vs. placebo 34.4%
  - % of participants losing ≥ 10% body weight: liraglutide 33.9% vs. placebo 15.4%

GLP-1 agonists (liraglutide)

Study 2

- 56- week double-blind RCT in 635 total participants (423 liraglutide vs 212 placebo)
- Participants included type 2 DM in addition to overweight/obesity as defined in Study 1
- Participants had an A1c of 7-10% & were actively treated with metformin, sulfonylurea, a glitazone or with a reduced-calorie diet and physical activity alone
- Mean baseline weight: 105.7kg $\pm$ 21.9 liraglutide vs. 106.5kg $\pm$ 21.3 placebo
- Avg weight loss from baseline: liraglutide 5.4% vs placebo 1.7%
- % of participants losing $\geq$ 5% body weight: liraglutide 49% vs. placebo 16.4%
- % of participants losing $\geq$ 10% body weight: liraglutide 22.4% vs. placebo 5.5%

GLP-1 agonists (liraglutide)

Study 3

- 56-week, RCT, placebo-controlled with initial 12-week run in period in 422 pts (212 liraglutide, 210 placbo)
- Initial 12 weeks participants were treated with a low-calorie diet (1200-1400 kcal/day)
- Participants who lost 5% baseline body weight or more during run-in period were randomized to liraglutide or placebo for 56 weeks
- Mean baseline weight: 100.4 kg $\pm$ 20.8 liraglutide vs. 98.7 kg $\pm$ 21.2 placebo
- Mean percent weight change from randomization to week 56: -6.2% liraglutide vs. -0.2% placebo
- Percentage of patients not gaining $\geq$5% body weight from randomization to week 56: 81.4% liraglutide vs. 48.9% placebo
- Percentage of patients achieving ≥5% weight loss from randomization to week 56: 50.5% liraglutide vs. 21.8% placebo

GLP-1 Agonists (semaglutide)

Name brand: Wegovy®

Approval date: June 4, 2021

Indication

- As an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adult patients with an initial body mass index of ≥30 kg/m^2 (obesity) or ≥27 kg/m^2 (overweight) in the presence of at least 1 weight-related comorbid condition (e.g. HTN, type 2 DM, or dyslipidemia)

Dosing

- Initial: 0.25 mg subQ once weekly for weeks 1-4; then 0.5 mg once weekly for weeks 5-8; then 1 mg once weekly for weeks 9-12; then 1.7 mg once weekly for weeks 13-16, then increase to semaglutide 2.4mg weekly
- Maint: 2.4 mg once weekly (If titration is not tolerated due to GI adverse events, consider delaying an escalation for 4 weeks)

MOA: long-acting analog of human GLP-1 (an incretin hormone) which increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, increases B-cell growth/replication, slows gastric emptying, and decreases food intake

Adverse effects: nausea, diarrhea, vomiting, constipation, abdominal pain, headache, fatigue, dyspepsia, dizziness, abdominal distension, eructation, hypoglycemia in patients with type 2 DM, flatulence, gastroenteritis, and gastroesophageal reflux disease, and nasopharyngitis

GLP-1 Agonists (semaglutide)

https://www.novomedlink.com/obesity/products/treatments/wegovy/dosing-administration/wegovy-dosing.html

GLP-1 Agonists (semaglutide)

Warnings

- Thyroid C-cell Tumors
- Acute Pancreatitis
- Acute Hypoglycemia
- Acute Kidney Injury
- Hypersensitivity Reactions
- Diabetic Retinopathy Complications in Patients with Type 2 Diabetes (lower than semaglutide)
- Heart Rate Increase
- Suicidal Behavior and Ideation

Contraindications

- Personal or family history of medullary thyroid carcinoma or in patients with MEN-2
- Known hypersensitivity to semaglutide or any of the excipients in semaglutide

Semaglutide may cause fetal harm

GLP-1 Agonists (semaglutide)

Cost

- All strengths: $404.71/dose

Data

- STEP trials (1-8, TEENS)
- STEP 1
  - 1961 participants; overweight-obese, no DM
  - 1305 semaglutide, 655 placebo
  - An average of 14.9% reduction in bodyweight from baseline during 68 weeks of treatment with semaglutide 2.4 mg weekly plus lifestyle intervention vs. 2.4% reduction in the placebo plus lifestyle group
- STEP 2
  - 1210 participants; overweight-obese with type 2 DM
  - Randomized 1:1:1 to receive semaglutide 1mg weekly, semaglutide 2.4mg weekly, or placebo
  - 404 semaglutide 2.4mg weekly, 403 semaglutide 1mg weekly, 403 placebo
  - Average weight reductions were 9.64%, 6.99%, and 3.42% with semaglutide 2.4 mg, 1.0 mg, and placebo, respectively

GLP-1 Agonists (semaglutide)

STEP 3

- 611 participants; overweight-obese, no DM
- Randomized to semaglutide 2.4mg weekly or placebo + behavioral health interventions
- 407 in semaglutide group, 204 in placebo group
- Average weight reduction after 68 weeks of treatment was 16.0% semaglutide vs 5.7% placebo
- Percentage of participants with > 5% weight loss was 86.6% semaglutide versus 47.6% placebo.

STEP 4

- 902 participants; overweight-obese, no DM
- All received semaglutide 2.4mg weekly for 20 weeks then randomized to placebo or semaglutide 2.4mg weekly for 48 more weeks
- 535 participants continued semaglutide; 268 switched to placebo
- Net weight loss: 17.4% semaglutide vs. 5% placebo
- Net weight change after randomization: -7.9% semaglutide vs. +6.9% placebo

GLP-1 Agonists (semaglutide)

STEP 5

- 304 patients (152 each group); overweight-obese, no DM
- Long-term study over 2 years of treatment with semaglutide 2.4mg weekly vs. placebo
- Percentage change in body weight: 15.2% semaglutide vs. 2.6% placebo
- Achievement of weight loss of ≥5% at week 104: 77.1% semaglutide vs 34.4% placebo

STEP 6

- 401 patients; in Japan and South Korea; overweight-obese with comorbidities (including DM)
- Randomized 2:1:1 to receive semaglutide 2.4mg weekly, 1.7mg weekly, or placebo
- 199 in semaglutide 2.4mg, 101 in semaglutide 1 mg, and 101 in placebo
- Percentage body weight reductions at 68 weeks: 13.2% semaglutide 2.4mg vs 9.6% semaglutide 1.7mg vs 2.1%
  placebo

GLP-1 Agonists (semaglutide)

STEP 7

- Completed, but not yet published

STEP 8

- 338 participants; overweight-obese with or without DM
- Semaglutide 2.4mg weekly vs. placebo vs Liraglutide 3mg weekly vs placebo
- Treatment duration of 68 weeks; randomized in a 3:1:3:1 manner
- 126 in semaglutide group, 127 in liraglutide group, and 85 total placebo
- At week 68, the estimated mean change in body weight was –15.8% with semaglutide and –6.4% with liraglutide

GIP/GLP1 Receptor Agonist (Tirzepatide)

Name brand: Zepbound ®

Approval date: Nov 2023

Indication: adjunct to a reduced-calorie diet & increased physical activity for chronic weight management in adult patients w/ an initial BMI of ≥30 kg/m^2 (obesity) or ≥27 kg/m^2 (overweight) in the presence of ≥1 weight-related comorbid condition (eg, ASCVD, dyslipidemia, HTN, OSA, type II DM)

Dose: Initial, 2.5 mg subQ once weekly for 4 weeks, then increase to 5 mg subQ once weekly; increase dosage in 2.5-mg increments after at least 4 weeks on the current dose; MAX, 15 mg subQ once weekly

MOA: long-acting analog of human GLP-1 (an incretin hormone) which increases glucose- dependent insulin secretion, decreases inappropriate glucagon secretion, increases B-cell growth/replication, slows gastric emptying, and decreases food intake

Adverse effects: nausea, diarrhea, decreased appetite, vomiting, constipation, dyspepsia, and abdominal pain

GIP/GLP1 Receptor Agonist (Tirzepatide)

Warnings

- Pancreatitis
- Hypoglycemia with Concomitant Use of Insulin Secretagogues or Insulin
- Hypersensitivity Reactions
- Acute Kidney Injury
- Severe Gastrointestinal Disease
- Diabetic Retinopathy Complications in Patients with a History of Diabetic Retinopathy
- Acute Gallbladder Disease

Contraindications

- Personal or family history of medullary thyroid carcinoma or inpatients with MENS-2
- Known serious hypersensitivity to tirzepatide or any of the excipients in MOUNJARO

Animal studies show tirzepatide may cause fetal harm

GIP/GLP1 Receptor Agonist (Tirzepatide)

Cost

- All strengths: $317.96/dose or $1271.84/month

Data

- SURMOUNT-1
- Phase 3 double-blind RCT of 2539 patients
- BMI of ≥30 kg/m^2 or ≥27 kg/m^2 or more and at least one weight-related complication, excluding diabetes
- Randomized 1:1:1:1 to receive once weekly tirzepatide 5mg, 10mg, 15mg or placebo for a total of 72 weeks
- 630 participants in 5mg group, 636 in 10mg group, 630 in 15mg group and 643 receiving placebo
- 20-week dose escalation period

GIP/GLP1 Receptor Agonist (Tirzepatide)

SURMOUNT-1

- % change in baseline weight at 72 weeks:
  - Tirzepatide 5mg, -15%
  - Tirzepatide 10mg, -19.5%
  - Tirzepatide 15mg, -20.9%
  - Placebo, -3.1%
- Weight reduction of 5% or more at week 72:
  - Tirzepatide 5mg, 85%
  - Tirzepatide 10mg, 89%
  - Tirzepatide 15mg, 91%
  - Placebo, 35%

GIP/GLP1 Receptor Agonist (Tirzepatide) Surgical Considerations

Delayed gastric emptying leading to increased risk of aspiration post surgical

Recommendation:

- Stop semaglutide/tirzepatide by at least 7 days before surgery (2 weeks after last dose)
- Stop liraglutide 2-3 days before surgery

Post-operative Respiratory Complications

- Potential for aspiration/pneumonitis, severe respiratory failure, postoperative hypoglycemia

Controversy

- American Society of Anesthesiologists consensus to hold dose for 7 days prior to surgery due to risk of delays in gastric emptying
- American Journal of Gastroenterology article found no substantial evidence to suggest delaying surgery due to GLP-1a use.

GLP-1 Agonists (semaglutide/tirzepatide)

Antidepressant/opioid antagonist (bupropion SR/naltrexone)

Name brand: Contrave®

Approval date: Originally recommended for FDA approval in December 2010, not approved until 2014

MOA: Combination

- Naltrexone is a pure opioid antagonist
- Bupropion is a relatively weak inhibitor of the neuronal reuptake of dopamine and norepinephrine
- The exact neurochemical effects of naltrexone/bupropion leading to weight loss are not fully understood. Effects may result from action on areas of the brain involved in the regulation of food intake: the hypothalamus (appetite regulatory center) and the mesolimbic dopamine circuit (reward system)

Dose: Initial: One tablet (naltrexone 8 mg/bupropion 90 mg) once daily in the morning for 1 week; increase as tolerated in weekly intervals: 1 tablet twice daily for 1 week; then 2 tablets in the morning and 1 tablet in the evening for 1 week; and then 2 tablets twice daily (maximum dose: 4 tablets/day [naltrexone 32 mg/bupropion 360 mg per day])

Consider discontinuation if weight loss is <4% to 5% of baseline after 3 months

Antidepressant/opioid antagonist (bupropion SR/naltrexone)

Warning

- [US Boxed Warning]: Naltrexone/bupropion is not approved for use in the treatment of major depressive or psychiatric disorders; it contains bupropion the same active ingredient in some other antidepressant medications. Antidepressants increase the risk of suicidal thinking and behavior in children, adolescents, and young adults (18 to 24 years of age) with major depressive disorder (MDD) and other psychiatric disorders

Concerns related to adverse effects:

- Accidental opioid overdose: May respond to lower opioid doses than previously used
- Acute opioid withdrawal: May precipitate symptoms of acute withdrawal in opioid-dependent patients
- Cardiovascular effects: May elevate heart rate, blood pressure and cause hypertension; use is contraindicated in patients w/uncontrolled HTN
- Hepatotoxicity: Cases of hepatitis, significant liver dysfunction, and transient, asymptomatic hepatic transaminase elevations have been observed with naltrexone use

Antidepressant/opioid antagonist (bupropion SR/naltrexone)

Concerns related to adverse effects (Cont.)

- Hypersensitivity reactions: Anaphylactoid/anaphylactic reactions have occurred, including pruritus, urticaria, angioedema, and dyspnea
- Neuropsychiatric effect: Although naltrexone/bupropion is not approved for smoking cessation, serious neuropsychiatric events have occurred in patients taking bupropion for smoking cessation, including changes in mood (eg, depression, mania), psychosis, hallucinations, paranoia, delusions, homicidal ideation, hostility, agitation, aggression, anxiety, panic, suicidal ideation, suicide attempt, and completed suicide
- Ocular effects: Bupropion may cause mild pupillary dilation, which in susceptible individuals can lead to an episode of narrow-angle glaucoma
- Seizures: Bupropion may cause a dose-related risk of seizures. Use is contraindicated in patients with a seizure disorder or a history of seizures, current or past diagnosis of bulimia or anorexia nervosa, or those undergoing abrupt discontinuation of alcohol, benzodiazepines, barbiturates, and antiseizure drugs

Antidepressant/opioid antagonist (bupropion SR/naltrexone)

Contraindications

- Hypersensitivity to bupropion, naltrexone, or any other component of the formulation; concomitant use of other bupropion-containing products (eg, including [but not limited to] Wellbutrin, Wellbutrin SR, Wellbutrin XL, Aplenzin, Zyban)
- Chronic opioid, opiate agonist (eg, methadone) or partial agonist (eg, buprenorphine) use
- Acute opioid withdrawal
- **Uncontrolled hypertension**
- **Seizure disorder or a history of seizures**
- Bulimia or anorexia nervosa
- Pts undergoing abrupt discontinuation of BZDs EtOH, barbiturates, or antiseizure drugs
- Concomitant use of MAOIs (concurrently or within 14 days of discontinuing the MAOI or naltrexone/bupropion)
- initiation of naltrexone/bupropion in a patient receiving linezolid or IV methylene blue

Cost: $6.25/tab

Antidepressant/opioid antagonist (bupropion SR/naltrexone)

Data

- Contrave Obesity Research Trials (COR-I, II, BMOD)
  - RCT, placebo controlled
  - Total patients studied in the 3 trials: 4,031
  - COR-I: 18-65yo with BMI of 30-45 kg/m^2 uncomplicated or 27-45 kg/m^2 complicated
  - COR-II: 18-65yo with BMI of 30-45 kg/m^2 uncomplicated or 27-45 kg/m^2 complicated
  - COR-BMOD: only trial to measure intensive behavioral modification
    - Average of 4.2kg weight loss over placebo
- Contrave showed 4-5kg more weight loss than placebo at 1 year
  - Contrave 48-66% of patients lost ≥5% of initial body weight vs 16-42% placebo
  - Contrave 25-42% of patients lost ≥10% of initial body weight vs 6-20% placebo

Antidepressant/opioid antagonist Surgical Consideration

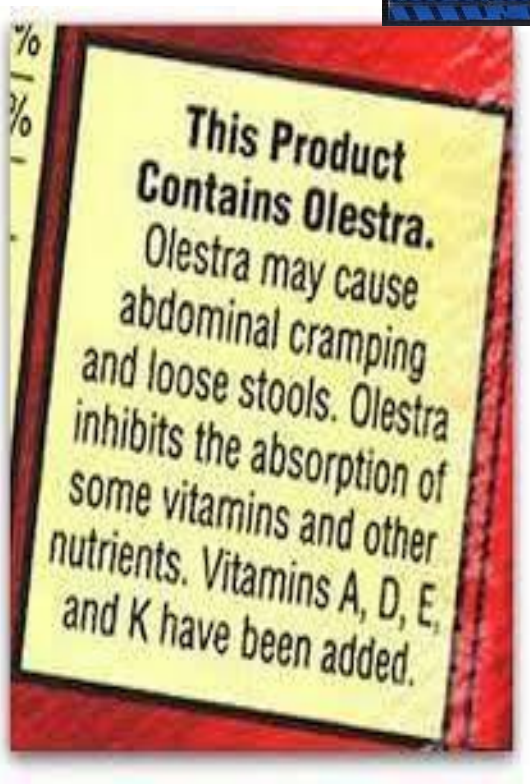
Increased opioid requirements

- Naltrexone (derivative of oxymorphone) blocks opioid receptor sites, specifically mu receptors
- Half life is 13 hours
- Mitigation Strategy: stop 3 days prior to surgery

Increased risk of seizures/Neuroleptic Malignant Syndrome

- Bupropion can lower seizure threshold as well as agonize dopamine binding sites
- Mitigation strategy: stop 3 days prior to surgery
- Titration strategy is important

Olestra/Olean



Lipase inhibitor (Orlistat)

Name brand: (Xenical)

(Alli) FDA approved: 1999

MOA: A reversible inhibitor of gastric & pancreatic lipases, thus inhibiting absorption of dietary fats by 30%

Dose:

- OTC: **Oral:** 60 mg 3 times daily with each main meal containing fat; maximum OTC dose: 180 mg/day
- Rx: 120 mg 3 times daily with each main meal containing fat (during or up to 1 hour after the meal); omit dose if meal is occasionally missed or contains no fat (manufacturer's labeling)
- **Note:** Some experts initiate with the 60 mg dose (Alli) to improve GI tolerability, or switch to the 60 mg dose if 120 mg is poorly tolerated
- Consider discontinuation if weight loss is <4% to 5% of baseline after 3 months

Lipase inhibitor (Orlistat)

Warnings

- Cholelithiasis: Substantial weight loss may increase the risk of cholelithiasis
- Hepatotoxicity: Cases of severe liver injury (some fatal) with hepatocellular necrosis or acute hepatic failure have been reported; liver transplantation has been required in some patients
- Increased urinary oxalate: Increased levels of urinary oxalate following treatment may occur in some patients; cases of oxalate nephrolithiasis and oxalate nephropathy with renal failure have been reported

Contraindications:

- Hypersensitivity to orlistat or to any component of the formulation; pregnancy; chronic malabsorption syndrome; cholestasis

Drug interactions: cyclosporine, levothyroxine, fat soluble vitamins

Cost: 60mg: $0.59/cap 120mg: $8.67/cap

Lipase inhibitor (Orlistat) Data

Cochrane meta-analysis including 11 RCTs using 120 mg Orlistat three times a day found:

- 2.7 kg (95% CI: 2.3 to 4/10/20083.1) or 2.9% (95% CI: 2.3 to 3.4) greater weight loss in the Orlistat group when compared to placebo
- Pooled results showed a larger number of participants in the Orlistat group achieved clinically significant weight loss, with 21% (95% CI: 19–24) & 12% (95% CI: 8 to 16) achieving ≥5% & ≥10% weight loss, respectively
- Orlistat has been shown to improve glycemic control in type-2 DM & reduce the risk of developing diabetes in overweight/obese individuals with impaired glucose tolerance
- Linked to small improvements in blood pressure and lower cholesterol than expected for the level of weight loss
- Orlistat may be useful in the management of NAFLD, menstrual dysfunction & overweight/obesity in adolescents
- Attrition rate is very high 90% stop taking at 1 year and >98% by 2 years

Lipase inhibitor Surgical Considerations

Decreased medication absorption can occur

- Rx meds levothyroxine, antiepileptic meds (gabapentin), anticoagulants
- Vitamins (fat soluble): D, E, K
- Little effect on opioid pain medications

Mitigation Strategy:

- Stop orlistat 1 day prior to surgery

Carbonic anhydrase inhibitor/stimula (topiramate/phentermine)

Name brand: Qsymia ®

MOA: Combination of

- Phentermine: A sympathomimetic amine with pharmacologic properties like amphetamines
- Topiramate: Effect on weight management may be due to its effects on appetite suppression & satiety enhancement and based on a combination of potential mechanisms

Dose: Initial: Phentermine 3.75 mg/topiramate 23 mg once daily for 14 days

- Increase dose as tolerated to phentermine 7.5 mg/topiramate 46 mg once daily for 12 weeks
- If ≥3% of baseline body weight has not been lost, either discontinue therapy with a gradual taper (eg, switch from daily dosing to every other day dosing for at least 1 week before discontinuing) or escalate the dose based on tolerability and patient preference
- Dose may be escalated to phentermine 11.25 mg/topiramate 69 mg once daily for 14 days and
- Then to a maximum dose of phentermine 15 mg/topiramate 92 mg once daily. Evaluate weight loss after 12 weeks on phentermine 15 mg/topiramate 92 mg; if ≥5% of baseline body weight has not been lost, discontinue therapy with a gradual taper (ie, switch from daily dosing to every-other-day dosing for at least 1 week before discontinuing)

Carbonic anhydrase inhibitor/stimulant (topiramate/phentermine)

Contraindications

- Hypersensitivity to phentermine, topiramate, or any component of the formulation or idiosyncrasy to sympathomimetic amines; hyperthyroidism; glaucoma; use during or within 14 days following monoamine oxidase inhibitor therapy; pregnancy

Warnings:

- CV effects: increase resting heart rate; monitor closely when starting or increasing dosage, and in patients with cardiac or cerebrovascular disease
- CNS effects: Cognitive dysfunction and psychiatric disturbances
- Dermatologic effects: Severe dermatologic reactions, including toxic epidermal necrolysis & Stevens-Johnson syndrome
- Hyperthermia: Associated (rarely) with severe oligohidrosis & hyperthermia
- **Renal calculus: Use is associated with kidney stone formation**

Carbonic anhydrase inhibitor/stimulant (topiramate/phentermine)

Warnings: cont….

- Metabolic acidosis (hyperchloremic, nonanion gap): May decrease serum bicarb concentrations, d/t increased renal bicarbonate loss
- Ocular effects: Topiramate has been associated with acute myopia & secondary angle-closure glaucoma in adults & children, typically w/i 1 month of initiation but may occur at any time
- Renal effects: May increase serum creatinine; peak increases from baseline were observed after 4 to 8 weeks of treatment. Changes in SCr (and GFR) w/ short-term use appear reversible w/ d/c; effects of long-term treatment on renal function are not known
- Suicidal ideation: Pooled analysis of trials involving various antiseizure medications (regardless of indication) showed an increased risk of suicidal thoughts/behavior (incidence rate: 0.43% treated patients compared to 0.24% of patients receiving placebo); risk observed as early as 1 week after initiation and continued through duration of trials (most trials ≤24 weeks)
- Cost: $8.46/cap

Carbonic anhydrase inhibitor/stimulant (topiramate/phentermine) Data

Phentermine/topiramate-ER was recommended for approval based:

- 2 x 1 year Phase 3 clinical trials: All groups received a low-intensity TLC program
- All underwent dose titration over 4 weeks to assigned dose followed by 52 weeks on drug or placebo
- EQUIP: n=1267: placebo controlled RCT w/o DM & w/ BMI ≥35 kg/m^2
  - Phentermine/topiramate-ER 3.75/23mg (starting dose) to 15/92mg (max dose)
  - 40% of participants withdrew
  - At max dose, mean 1y weight loss was 10.9% active vs. 1.6% of initial weight for placebo
  - 67% of patients given the max dose lost ≥5% of initial weight & 47% lost ≥10% of initial weight, compared w/ 17% & 7%, for placebo
- CONQUER: n=2487 & Sequel-extension to CONQUER
  - CONQUER randomized a higher-risk sample of adults w/ BMI 27–45 kg/m^2 and ≥2 obesity-associated comorbid conditions, to placebo or phentermine/topiramate-ER
  - 31% of participants withdrew
  - 1 year weight loss was 8.1 kg (7.8%) w/ the recommended dose & 10.2 kg (9.8%) with the max dose, vs. 1.4 kg (1.2%) w/ placebo
  - 62% (recommended dose) & 70% (max dose) lost ≥5% of initial weight vs. 21% for placebo, w/ 37%, 48%, & 7% respectively losing ≥10% of initial weight
  - SEQUEL an extension to CONQUER, followed 78% up to 108 weeks
  - 84% completed their 2nd year of treatment with sustained weight loss of 9.3% and 10.5% at the recommended & max doses, respectively, vs. 1.8% for placebo

Carbonic anhydrase inhibitor/stimulant (topiramate/phentermine) Data

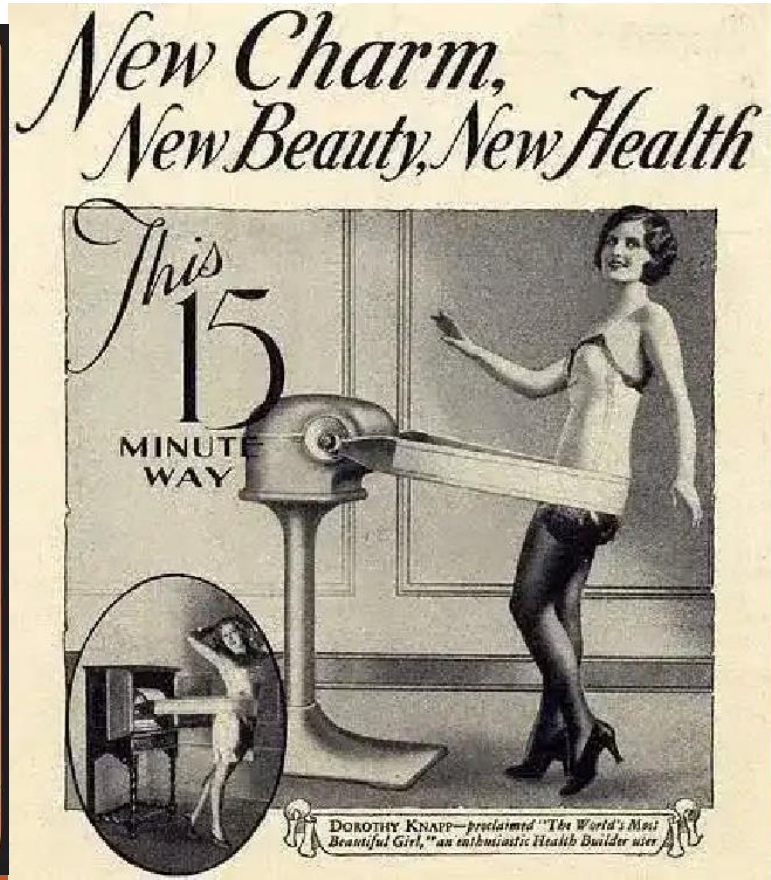
Surgical Considerations:

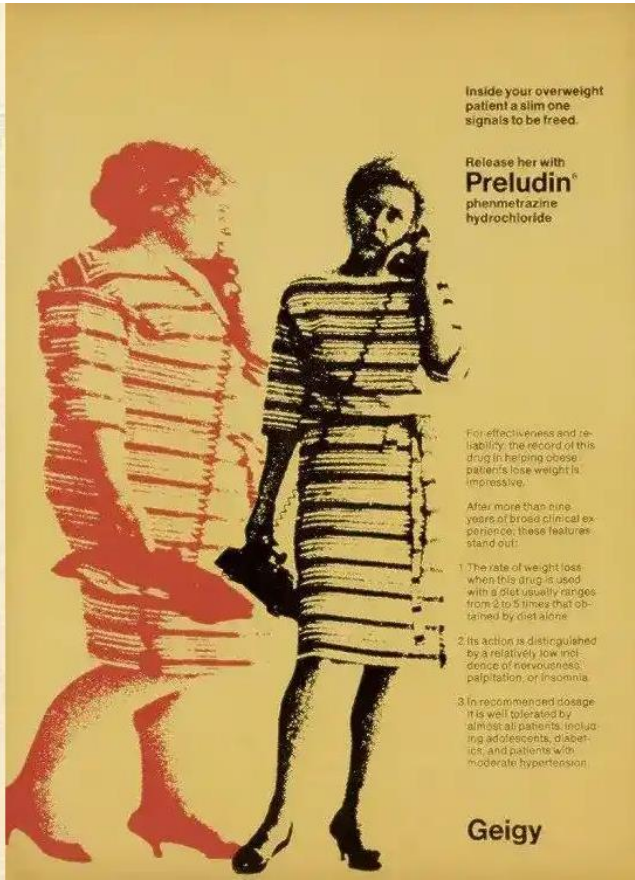
- See risk associated with phentermine
- Higher risk of metabolic acidosis post surgical related to increased risk of bicarbonate secretion d/t topiramate
- Higher risk of electrolyte abnormalities post surgery
  - Increased Cl, risk of hyperchloremic acidosis
  - Decreased PO4
  - Decreased K
  - Hyperammonemia
- Mitigation:
  - See topiramate and phentermine slide

Lorcaserin (Belviq & Belviq XR)

No longer on the market

Removed July 2020





Off-Label/Unlabeled Medications

Nibble on a cookie about an hour before lunch.

Sugar keeps your energy up—and your appetite down.

Willpower fans, the search is over! And guess where it's at? In sugar! Sugar works faster than any other food to turn your appetite down, turn energy up.

Spoil your appetite with sugar, and you could come up with willpower—the willpower you need to eat less, and maybe even weigh less.

Sugar . . . only 18 calories per teaspoon, and it's all energy.

Sugar Information
General Post Office Box 94, New York, N. Y. 10001

Other Off-label Medications for Obesity Treatment

Bupropion (Wellbutrin®): Selective Norepinephrine/Dopamine Reuptake Inhibitor

- A pooled analysis of 3 studies ranging from 6 to 12 months showed additional weight loss relative to placebo of 2.8 kg in patients receiving 400mg/d bupropion, with total weight loss of 4.4 kg
- Surgical considerations discussed during Contrave portion

Pramlintide (Symlin®): Synthetic analogue of human amylin, administered at mealtimes as an adjunct to insulin for Type 1 & 2 DM

- A meta-analysis of 8 studies in pts w/ type 2 DM & obese non-DM pop found add weight loss relative to placebo of about 2.2 kg for both groups
- Surgical considerations: increased risk of hypoglycemia especially if used with insulin
- Delays gastric emptying
- Hold day of surgery

Metformin (Glucophage®): Biguanide that produces small sustained weight losses of about 2% relative to placebo

- Usefulness as monotherapy for obesity treatment is limited, but its salutary effects on body weight make it a good choice when other indications warrant its prescription
- A meta-analysis examining the effect of medications for attenuation of antipsychotic weight gain found an approximate 3 kg additional weight loss relative to placebo attributable to metformin
- Surgical considerations: Increased risk of lactic acidosis with the following risk factors: renal impairment, use with carbonic anhydrase inhibitors, ≥65yo, having a radiological study with contrast, surgery and other procedures, hypoxic states, excessive EtOH intake, hepatic impairment
- Hold metformin day of surgery, restart after stable renal function

Other Off-label Medications for Obesity Treatment

Carbonic Anhydrase Inhibitors

- **Zonisamide (Zonegran ®):**
  - 12-month RCT of 225 adults, with 97% follow-up
  - 400mg dose led to significantly greater weight loss than placebo (6.8% vs. 3.7%), as well as a greater proportion losing ≥5% and ≥10% of initial weight
- **Topiramate (Topiramate ®):**
  - Meta-analysis that included 3,320 patients with obesity from 10 studies
  - Topiramate (64 mg – 400 mg/day as a weight loss agent) to placebo over periods of 16 – 60 weeks
  - Mean weight loss experienced by patients taking topiramate was 5.34 kg greater than with placebo
  - Risk of study withdrawal due to an adverse event was greater for topiramate treated patients (OR: 1.95) and was associated with a higher dosage

Surgical Considerations:

- Increased risk of lactic acidosis post surgery
- If used as anticonvulsant, do not hold prior to surgery

Off-label Medications for Obesity Treatment

SGLT-2 inhibitors (canagliflozin, dapagliflozin, empagliflozin)

- Trials of 12 – 52 weeks duration, with dapagliflozin, canagliflozin, weight loss of 2 – 3 kg was seen
- In a meta-analysis of trials of one to two years duration, SGLT2 inhibitors (canagliflozin, dapagliflozin, and empagliflozin) showed a weight loss at two years compared to placebo of –2.99 kg
- Causes loss of 60-100g of glucose per day in the urine (equal to 204-304kcal/day)
- Surgical considerations: Increased risk of ketoacidosis and lower limb amputations (canagliflozin) due to metabolic stressful events
- Prevention: d/c therapy 3-5 days prior to surgery to reduce risk

Testosterone Replacement Therapy

- Testosterone supplementation in eugonadal men (total testosterone 350-400 ng/dL or higher) leads to no improvement in weight loss
- Significant controversy and mixed results regarding the CV effects of testosterone therapy
- Surgical considerations: Previously thought that preoperative TRT increased postoperative in hospital mortality in noncardiac surgery, but recent data has not found a correlation

Other Off-label Medications for Obesity Treatment

HCG:

- No role in weight loss therapy, ineffective and has serious safety concerns
- Meta-analysis published in 1995 reviewed the use of intramuscular HCG in 24 studies to include 14 RCTs
- Authors concluded that HCG was no more effective than a placebo or diet alone for weight loss, fat redistribution, or a sense of well-being

Cyanocobalamin:

- No studies evaluating weight loss w/ vitamin B-12 inj, tabs, SL pills, or drink
- No weight loss should be anticipated because of the use of exogenous vitamin B-12

Thyroid hormones:

- Normalization of the hypothyroid state is associated with small losses of weight (less than 1 kg)
- Treatment of euthyroid patients to hyperthyroid levels has not been reported outside of control groups in early phase clinical trials

Surgical consideration: None

Questions

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