Pharmacological Management of Obesity:

An Endocrine Society Clinical Practice Guideline
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I. Overview of Pharmacological Management of the Obese Patient: An Endocrine Society Clinical Practice Guideline

• Highlights and Key Recommendations
• Patient Treatment Plans

II. Case Discussion
I. Overview of Pharmacological Management of the Obese Patient: An Endocrine Society Clinical Practice Guideline
First Guideline of its Kind

Blueprint on:

- Medical management of the disease of obesity
- Clinical encounter with overweight and obese patients
- Rationale for pharmacologic treatment of obesity
- Care of the patient who is overweight or obese
- Drugs that cause weight gain and alternative drugs that promote weight neutrality or weight loss
- Off-label use of drugs for weight loss
The Role of Medications in Weight Loss

They do not “work on their own.”

- Medications amplify the effect of behavioral changes to produce consumption of fewer calories.
- Addition of a weight loss medication to a lifestyle program will likely result in greater weight loss.
Fundamentals of Care

- Diet
- Exercise
- Behavioral Modification
- Pharmacotherapy
- Bariatric Surgery

Adjuncts only

Fundamental to all obesity management
Clinician Role in Patient Encounter

Perform annual screening for major chronic conditions associated with obesity in all adult patients with a BMI $\geq 30$ kg/m$^2$

- T2DM
- Cardiovascular disease
- Hypertension
- Hyperlipidemia
- Obstructive sleep apnea
- Nonalcoholic fatty liver disease
- Osteoarthritis
- Major depression

Adhere to national cancer screening guidelines

Obese individuals are at increased risk for many malignancies

Identify and screen for secondary causes of obesity

- Family history
- Sleep disorders
- Disordered eating
- Genetics
- Environmental
- Socioeconomic

Identify contributing factors

Adhere to AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults

Identify medications that contribute to weight gain and prescribe alternatives

Formulate treatment plan based on diet, exercise, and behavior modifications
Criteria for Using Approved Medications

Adjunct to an energy deficient diet, increased physical activity and behavior modification

BMI: <18.5  18.5-24.9  25.0-29.9  30.0-34.9  ≥35  >40

BMI of ≥27 kg/m² with ≥1 comorbidity

BMI of ≥30 kg/m² with no comorbidities

www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/
Frequent Patient Follow-up is Key

All patients prescribed weight loss medications:

- At least monthly for first 3 months
- Then at least every 3 months

Best weight loss outcomes occur with frequent face to face visits (16 visits per year average)
Weight Loss Drugs: Dosage and Duration

For situations or times of year where lifestyle factors promote weight regain

Long-term Obesity Treatment:
Start with lowest dose

Phentermine/topiramate 7.5mg/46 mg
Lorcaserin 10 mg bid
Orlistat 120 mg tid
Orlistat OTC 60 mg tid

Intermittent Use

For situations or times of year where lifestyle factors promote weight regain
Several months on, one month off
## Old Treatment Paradigm

**Treat Weight LAST**

<table>
<thead>
<tr>
<th>Dyslipidemia</th>
<th>HTN</th>
<th>IGT</th>
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<tbody>
<tr>
<td>Lipid panels</td>
<td>Blood Pressure</td>
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### Monitor
- Lipid panels
- Lipoproteins subsets

### Diet
- ↓ Total fat
- ↓ Chol.
- ↑ Fiber

### Meds
- Statins
- Fibrates
- Resins
- Niacin
- Central acting Renal effective Peripherally acting diuretics
- Thiazide diuretics
- Insulin
- Sulfonylureas
- Glidizones
- Absorption agents

## New Treatment Paradigm

**Treat Weight FIRST**

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<thead>
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<tr>
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<td>Glycemic index diet</td>
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| Meds | Orlistat, phentermine, phentermine/topiramate, lorcaserin | Sodium | ↑ Fiber
- Diabetic diet |

### Monitor
- Weight and BMI

### Diet
- Any diet patient will adhere to

### Exercise
- 150 minutes of moderate-intensity aerobic activity/wk and muscle-strengthening activities on > 2 days/wk

### Meds
- Statins
- Fibrates
- Resins
- Niacin
- Central acting Renal effective Peripherally acting diuretics
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- Sulfonylureas
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### Overweight/Obesity

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Patient Treatment Plans
Criteria for Using Approved Medications

Dual benefit of weight loss and glycemic control

- Metformin
- Glucagon-like Peptide-1 (GLP-1) Agonists:
  - Exenatide
  - Liraglutide
- New class SGLT-2 Inhibitors:
  - Dapagliflozin
  - Canagliflozin

RECOMMENDED
Overweight/Obese Patient with T2DM

Who is on medication which promote weight gain: insulin, sulfonylureas, and other insulin secretagogues, and thiazolidinediones (TZD’s)

1. Embark on weight loss plan:
   - Diet
   - Exercise

2. Maximize metformin

3. Add in GLP-1
   - Liraglutide or
   - Exenatide

4. Taper
   - Insulin
   - Sulfonylureas

5. Taper TZD
   - (pioglitazone)
   - Consider SGLT2 inhibitor
Overweight/Obese Patient with T2DM

Who is on insulin

1. Embark on weight loss plan:
   • Diet
   • Exercise

2. Use basal insulin, avoid premixed insulins, prevent hypoglycemia

3. Combination therapy with
   • Metformin
   • Pramlintide
   • OR GLP-1 agonists

4. Combine basal insulin with a DPP-4
   • (sitagliptin)
Overweight/Obese Patient with T2DM

Who is hypertensive, has depression on insulin, and a sulfonylurea

1. Embark on weight loss plan:
   - Diet
   - Exercise

2. Add in GLP-1
   - Liraglutide or
   - Exenatide

3. Taper
   - Insulin and
   - Sulfonylureas

4. Taper TZD
   - (pioglitazone)
   - Add a DPP-4
   - (sitagliptin)

5. Switch beta-blocker with an ace inhibitor

6.
Overweight/Obese Patients with CVD

Use agents without cardiovascular signals (increased blood pressure and pulse):

- **Orlistat**
- **Lorcaserin**
  - Lower risk of increased blood pressure than phentermine/topiramate
Summary

- First guideline that specifically names anti-obesity medications and recommended doses
- Patient selection criteria:
  - BMI ≥27 kg/m² with one comorbidity
  - BMI ≥30 kg/m² with no comorbidities
- Diet, exercise and behavior modification is the foundation of any weight management plan
- Provides a blueprint on medications that cause weight gain and their alternatives
- New paradigm: treat weight first, then comorbid condition(s)
III. Case Discussions
Case 1
55-year-old male with metabolic syndrome

FH:
DM and CAD

Medications
- Atenolol 50 mg
- Valsartan
- Glipizide 5 BID
- Pioglitazone
- Metformin 500 BID
- Atorvastatin
- Insulin - glargine 20 units/night

CC:
Cannot lose weight despite personal training 3x/week

Lab Data
- Weight 264 lbs
- Height 5’ 10”
- BMI 38 kg/m²
- WC 45 in
- BP 150/95
- HbA1c 7.2%
- FBG 150-175 mg/dL
- TC 220 mg/dL
- TG 300 mg/dL
- LDL-C 130 mg/dL
- HDL-C 40 mg/dL
An obese, 55 year old man with metabolic syndrome due to hypertension, diabetes and elevated lipids is having trouble losing weight on his own through lifestyle interventions. He has hired a personal trainer, working out three times a week, to no avail. He takes seven medications to control his comorbidities.

Path number one for the provider would be to evaluate his medications to see if there are any that exacerbate weight gain, and to consider alternatives.

He is a candidate for bariatric surgery because of his Type 2 DM and BMI between 35 and 40. Adding obesity pharmacology to his exercise routine with a low-calorie, high-protein diet would be an important first step.
The medications to stop and/or reduce while undergoing weight loss with a high protein / low-carbohydrate diet, would be the anti hyperglycemic agents: insulin, glipizide and pioglitazone. Slowly reduce these medications based on blood glucose, one at a time, by one-half dose at a time.

During downtitration, Metformin can be maximized to 1000 mg a day, and a GLP-1 agonist like liraglutide or exenatide could be added.

Continue to downtitrate antihyperglycemic medications that cause weight gain until most or all have been stopped.

He should also be weaned off atenolol if possible, replacing with another agent such as a thiazide diuretic.

Should weight loss plateau after these changes, obesity pharmacology can be added such as lorcaserin or phentermine/topiramate combination.
Case 1 – Questions

55-year-old male with metabolic syndrome

Before starting a low-calorie diet, you would stop:
1. Pioglitazone
2. Glipizide
3. Atenolol
4. Metformin
5. Insulin

Which of his medications cause weight gain?
1. Atenolol
2. Diovan
3. Glypizide 5 BID
4. Actos
55-year-old male with metabolic syndrome

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1. Pioglitazone
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4. Metformin
5. Insulin

Which of his medications cause weight gain?

1. Atenolol
2. Diovan
3. Glipizide 5 BID
4. Actos
Case 2

61-year-old female with post menopausal weight gain

- Severe obesity, referred for surgery
- Asthma, arthritis, fibromyalgia
- Undiagnosed high blood pressure

<table>
<thead>
<tr>
<th>FH Obesity</th>
<th>Lab Data</th>
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<tbody>
<tr>
<td>Medications</td>
<td></td>
</tr>
<tr>
<td>• Zafirlukast</td>
<td>• Weight 200 lbs</td>
</tr>
<tr>
<td>• Albuterol inhaler</td>
<td>• Height 5’ 5”</td>
</tr>
<tr>
<td>• Metoprolol</td>
<td>• BMI 33 kg/m²</td>
</tr>
<tr>
<td>• Loratadine</td>
<td>• WC 34 in</td>
</tr>
<tr>
<td>• Etodolac</td>
<td>• BP 160/95</td>
</tr>
<tr>
<td>• Nortriptyline</td>
<td>• HbA1c 5.9</td>
</tr>
<tr>
<td>• Paroxetine</td>
<td>• FBG 105 mg/dL</td>
</tr>
<tr>
<td>• Vitamin B, MVI, Calcium</td>
<td>• TC 250 mg/dL</td>
</tr>
<tr>
<td></td>
<td>• TG 260 mg/dL</td>
</tr>
<tr>
<td></td>
<td>• LDL-C 150 mg/dL</td>
</tr>
<tr>
<td></td>
<td>• HDL-C 50 mg/dL</td>
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</tbody>
</table>
Case 2 – Discussion

61-year-old female with post menopausal weight gain

Weighing 200 pounds on a 5’ 5” frame, this 61 year old woman is severely obese and has been referred for bariatric surgery. She has gained weight steadily since the onset of menopause and is on an array of medications to control her comorbidities (zafirlukast, albuterol inhaler, loratadine, etodolac, nortriptyline, metoprolol and paroxetine).

With a BMI of 33 she does not meet the surgical criteria (BMI ≥40, or 35 with comorbidities) therefore, she is a candidate for diet, exercise and behavior therapy with or without a pharmacological option. She is also on an anti-depressant (paroxetine) which can cause weight gain. Replace paroxetine with a celexa or lexapro.
Case 2 – Discussion (cont.)

Her asthma and arthritis will improve with weight loss, as will her high blood pressure and her metoprolol can be weened off as she loses weight. Elevated lipids will also improve.

If she is on phentermine/topiramate combination, blood pressure must be monitored carefully as it is already elevated.

If lorcaserin is considered use with extreme caution due to the risk of serotonin syndrome because she is on a SSRI. Also pertinent for serotonin-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), triptans, bupropion, dextromethorphan, St. John’s Wort).

Her lipids and asthma suggests she is in a chronic state of inflammation which may also improve with weight loss.
Case 2 – Questions

61-year-old female with postmenopausal weight gain

Which comorbidities should improve with weight loss?
1. Asthma
2. Arthritis
3. Fibromyalgia
4. Hypertension

Which of her medications can cause weight gain?
1. Zafirlukast
2. Loratadine
3. Etodolac
4. Paroxetine
Case 2 – Questions

61-year-old female with postmenopausal weight gain

Which comorbidities should improve with weight loss?
1. Asthma
2. Arthritis
3. Fibromyalgia
4. Hypertension

Which of her medications can cause weight gain?
1. Zafirlukast
2. Loratadine
3. Etodolac
4. Paroxetine
Case 3
27-year-old female post breast feeding weight gain

Medications
- Prenatal vitamins

Lab Data: Baseline
- Weight was 150 lbs
- Weight now 185 lbs
- Height 5’ 5”
- BMI was 25 kg/m²
- BMI now 31 kg/m²
- All other parameters normal

35 lb weight gain from Overweight to Obese
Case 3 - Discussion

27-year-old female post breast feeding weight gain

A 27 year old woman has gained 35 pounds since stopping breast feeding several months ago. Her pre-pregnancy weight was 150 at a BMI of 25. She now weighs 185 with a BMI of 31 and she is looking to get back to her pre-pregnancy weight. All her other parameters are normal.

With a BMI of 31 she is a candidate for diet, exercise, behavioral therapy - with or without an obesity medication.

She is a candidate for either phentermine/topiramate combination or lorcaserin.

A weight loss of 10% is what would be considered successful (~ 20 lbs). It is conceivable that she could achieve pre-pregnancy weight loss. At that point a decision would have to be made with patient and the provider as to if and when to stop the obesity medication, and monitor for weight regain.
Case 3 – Questions

27-year-old female post breast feeding weight gain

If this patient reaches her pre-pregnancy weight of 150 pounds, what will be her % excess weight loss?
1. 19%
2. 100%
3. 40%
4. 50%

If this patient reaches her pre-pregnancy weight of 150 pounds, what will be her % total weight loss?
1. 19%
2. 100%
3. 40%
4. 50%
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1. 19%
2. 100%
3. 40%
4. 50%

If this patient reaches her pre-pregnancy weight of 150 pounds, what will be her % total weight loss?

1. 19% (35 divided by 185 = 19%)
2. 100%
3. 40%
4. 50%
Case 4

50-year-old female post gastric bypass weight gain

**CC:**
- Lost 100 pounds with surgery
- 2 years post surgery 40 lb gain
- Blood glucose creeping up
- Pouch dilatation

**Hx:** Diabetes, for 3 years pre-surgery

<table>
<thead>
<tr>
<th>Height 5'4&quot;</th>
<th>BMI</th>
<th>1 Year post Surgery</th>
<th>2 Years Post Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-surgery</td>
<td>41 kg/m²</td>
<td>24 kg/m²</td>
<td>31 kg/m²</td>
</tr>
<tr>
<td>Weight</td>
<td>240 lbs</td>
<td>140 lbs</td>
<td>180 lbs</td>
</tr>
<tr>
<td>FBG</td>
<td>135 mg/dL</td>
<td>94 mg/dL</td>
<td>120 mg/dL</td>
</tr>
<tr>
<td>HbA1c</td>
<td>10%</td>
<td>5%</td>
<td>6.5%</td>
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**Pre-op Medications**
- Metformin
- Glipizide

40 lb weight gain in 2 years from Normal to Pre-diabetes
Case 4 – Discussion

50-year-old female post gastric bypass weight gain

A 50 year old woman underwent a successful gastric bypass two years earlier. She has gained 35 pounds since her surgery. Her diabetes, which resolved after surgery, is back to a pre-diabetes level.

She should be monitored on a high protein, low-carbohydrate diet\(^1\), and given an exercise regimen.

Consider re-starting metformin and perhaps adding a GLP-1 agonist as well.

Follow-up on her metformin and GLP-1. She should be losing 1-2 pounds of weight loss per week. After 3 months, she should have lost 12-20 pounds; if she has not - consider phentermine/topiramate combination or lorcaserin.
Case 3 – Questions
50-year-old female post gastric bypass weight gain

This patient should be placed back on:
1. Metformin
2. Glipizide
3. Both above
4. None of the above

What other information is needed to work up this case?
1. More diet history
2. Upper GI series
3. CT scan of abdomen
4. MRI of abdomen
Case 3 – Questions

50-year-old female post gastric bypass weight gain

This patient should be placed back on:

1. Metformin
2. Glipizide
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