

Pharmacotherapy for the Obese Patient

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KEYWORDS

- Obesity • Pharmacotherapy • Orlistat
- Phentermine • Sibutramine

Obesity (body mass index [BMI] ≥ 30) and overweight (BMI ≥ 25) are the most common nutritional disorders in the United States, affecting almost two-thirds of the US population.¹ Obesity and overweight are associated with multiple coexisting conditions, some of which include hypertension, glucose intolerance, hyperlipidemia, and obstructive sleep apnea.²

Historically, the treatment of obesity has been extremely difficult. An efficient and beneficial treatment for obesity, which will satisfy the desires of most patients for rapid resolution and provide long-term results, is not available. As a caloric deficit of 3500 kcal is necessary to lose 1 lb of adipose tissue and most experts recommend losing no more than 1 to 2 lb/wk, weight loss is typically slow, and recidivism is very high. Therefore, obesity is a chronic medical condition, and treatment should be initiated with the expectation that long-term therapy will be needed.³

Early weight loss medications were proposed as short-term adjuncts to diet and exercise regimens, in the hopes that they would aid in initial weight loss and help patients reach “ideal body weight.” Unfortunately, these short-term regimens were unsuccessful, and the literature contains multiple reports of failed weight loss regimens.^{4–7} Currently, very few drugs are approved by the Food and Drug Administration (FDA) for the treatment of obesity in adults, and each must be used as part of a comprehensive weight loss program including diet and physical activity. These and other agents (**Table 1**) have been studied for weight loss, but all have major drawbacks and usually result in weight gain after discontinuation.^{3,8–10} Attrition rates approach 30% to 40% for most weight loss medications due to side effects and a lack of efficacy.¹⁰ Though behavioral modification incorporating dietary restrictions and appropriate exercise is the preferred treatment, the pharmacologic treatment of obesity is an area of continued research and development.

The National Institutes of Health recommend that nonpharmacologic therapies should be attempted for at least 6 months before drug therapy is considered (Strength of Recommendation [SOR] C).¹¹ Initial choice of a weight loss medication is empirical,

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Category	Medications	FDA Approved for Obesity Treatment
Adrenergic agents	Benzphetamine	Yes
	Diethylpropion	Yes
	Phendimetrazine	Yes
	Phentermine	Yes
Serotonergic agents	Dexfenfluramine	Yes
	Fenfluramine	Yes
	Fluoxetine	No
Adrenergic/serotonergic agents	Sibutramine	Yes
Lipase inhibitors	Orlistat	Yes
Antidepressants	Bupropion	No
Anticonvulsants	Zonisamide	No
	Topiramate	No
Cannabinoid antagonists	Rimonabant	No

Data from Refs. ^{3,8,9,23}

considering underlying medical conditions, concurrent medications, potential drug interactions, approval for long-term use, and cost. Patients without a weight loss of at least 2 kg in the first month of treatment should be reassessed, evaluating adherence to diet and exercise recommendations and considering a dosage adjustment (SOR C).³ If weight loss is still minimal, therapy should be discontinued (SOR C). Combination therapy (ie, sibutramine plus orlistat) has not been shown to enhance weight loss, may increase side effects, and is not recommended outside clinical trials (SOR B).

When considering an initial weight loss medication or evaluating patients who have failed a weight loss regimen, it is also important to determine if the patient is taking any agents that can promote weight gain.¹² For example, psychiatric agents are commonly associated with weight gain and include antidepressants (selective serotonin reuptake inhibitors [SSRIs], tricyclic antidepressants), antipsychotics (especially clozapine, olanzapine, risperidone), anticonvulsants (valproic acid, carbamazepine, gabapentin), and lithium. Antidiabetic agents, such as insulin, sulfonylureas (glyburide, glipizide), and thiazolidinediones (rosiglitazone, pioglitazone), commonly cause weight gain. Corticosteroids, centrally acting antihypertensive agents (methyldopa, clonidine), and depomedroxyprogesterone acetate have also been associated with weight gain. Weight loss may be more successful if these agents are discontinued or substituted for more weight neutral agents (SOR C). In the case of diabetes control, therapy may be switched to a regimen that includes metformin, exenatide, or pramlintide.^{3,9} Metformin may also be used to promote weight loss in patients who gain more than 10% of their pretreatment body weight when taking antipsychotic medications (SOR A).¹³

APPETITE SUPPRESSANTS

Most appetite suppressants work by increasing norepinephrine, dopamine, serotonin, or some combination of these in the central nervous system.³ These agents are typically classified as noradrenergic agents (ie, benzphetamine, diethylpropion,

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