Pharmacotherapy for Obesity

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KEYWORDS

• Obesity • Weight management • Pharmacotherapy • Orlistat
• Phentermine/topiramate ER • Lorcaserin • Naltrexone SR/bupropion SR
• Liraglutide

KEY POINTS

- Obesity treatment requires a multidisciplinary approach, which can include pharmacotherapy.
- There are several obesity medications approved by the Food and Drug Administration and the newer agents have been approved for long-term therapy.
- Successful pharmacotherapy depends on tailoring treatment to a patient's behaviors and comorbidities.

INTRODUCTION

Successful treatment of obesity requires a multidisciplinary approach, including diet, exercise, and behavioral modification. Even with significant lifestyle changes, weight loss is a challenge for many patients, as reduced calorie consumption and increased energy expenditure are counteracted by adaptive physiologic responses.[1–3] Reduction in body mass causes an increase in appetite and a decrease in energy expenditure, which is out of proportion to the weight loss. These changes are associated with alterations in a range of hormones.[4,5]

According to the 2013 American Heart Association, American College of Cardiology, and The Obesity Society Guideline for the Management of Overweight and Obesity in Adults, pharmacotherapy for the treatment of obesity can be considered if a patient has

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- A body mass index (BMI) $\geq$30 kg/m^2
- A BMI $\geq$27 kg/m^2 with weight-related comorbidities, such as hypertension, type 2 diabetes, dyslipidemia, and obstructive sleep apnea.[6]

In 2015, the Endocrine Society published clinical practice guidelines on pharmacologic management of obesity.[7] These evidence-based guidelines include recommendations for individualized weight management and ongoing evaluation of medication efficacy.

The development and approval of new antiobesity medications is challenging. As many weight loss drugs have been withdrawn over the years due to side effects and adverse events, the Food and Drug Administration (FDA) has strict criteria for medication approval.[8,9] A new agent must induce at least 5% statistically significant placebo-adjusted weight loss at 1 year or 35% or more of patients must achieve at least 5% weight loss (which must be at least twice that induced by placebo). The FDA also requires evidence that a medication improves metabolic biomarkers including blood pressure, lipids, and glycemia.

The following are the 6 most widely prescribed obesity medications approved by the FDA:

- Phentermine
- Orlistat
- Phentermine/topiramate extended release (ER)
- Lorcaserin
- Naltrexone sustained release (SR)/bupropion SR
- Liraglutide 3.0 mg (**Table 1**)

Most of the antiobesity medications affect appetite mechanisms, signaling through serotonergic, dopaminergic, or noradrenergic pathways. They primarily target the arcuate nucleus of the hypothalamus to stimulate anorexigenic pro-opiomelanocortin (POMC) neurons, which promote satiety. Orlistat is the only medication that is not significantly absorbed systemically; it blocks absorption of fat calories.

In the past, medications for obesity were used as short-term treatment. However, newer agents have been approved for long-term therapy, as obesity is now considered to be a chronic disease.[10] Phentermine/topiramate ER, lorcaserin, naltrexone SR/bupropion SR, and liraglutide 3.0 mg are indicated for chronic weight management, as an adjunct to a reduced-calorie diet and increased physical activity.[11–14] Phentermine is the only medication approved as a short-term adjunct,[15] and orlistat has the added indication to reduce risk for weight regain after prior weight loss.[16]

The aim of this article was to review current pharmacotherapy for obesity. Medications approved for weight management should be viewed as useful additions to diet and exercise for patients who have been unsuccessful with lifestyle changes alone.

PHENTERMINE

Phentermine was approved by the FDA in 1959 and has been the most commonly prescribed antiobesity medication in the United States. It was approved only for short-term use (3 months) as there are no long-term safety trials of phentermine monotherapy; however, many practitioners prescribe phentermine for longer durations as off-label therapy for continued weight management. In addition, phentermine was approved in combination with topiramate ER for chronic weight management in 2012. Other antiobesity medications, such as diethylpropion and phendimetrazine are also available in the United States, but use and data are minimal.