Obesity Pharmacotherapy

Katherine H. Saunders, MD, DABOM*, Devika Umashanker, MD, MBA, Leon I. Igel, MD, DABOM, Rekha B. Kumar, MD, MS, DABOM, Louis J. Aronne, MD, DABOM, FTOS

KEYWORDS

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

KEY POINTS

- Although diet, physical activity, and behavioral modifications are the cornerstones of weight management, weight loss achieved by lifestyle modifications alone is often limited and difficult to maintain.
- Pharmacotherapy for obesity can be considered if patients have a body mass index (BMI) of 30 kg/m^2 or greater or a BMI of 27 kg/m^2 or greater with weight-related comorbidities.
- The 6 most commonly used antiobesity medications are phentermine, orlistat, phentermine/topiramate extended release, lorcaserin, naltrexone sustained release (SR)/bupropion SR, and liraglutide 3.0 mg.
- It is important for primary care providers to be familiar with the pharmacotherapy available to patients who cannot lose weight and sustain weight loss with lifestyle interventions alone.
- Successful pharmacotherapy for obesity depends on tailoring treatment to patients' behaviors and comorbidities as well as close monitoring of efficacy, safety, and tolerability.

INTRODUCTION

Diet, physical activity, and behavioral modifications are the cornerstones of weight management.[1] However, weight loss achieved by lifestyle modifications alone is often limited and difficult to maintain. Reduced caloric intake and increased energy

Disclosure Statement: K.H. Saunders, D. Umashanker, and L.I. Igel have no conflicts of interest. R.B. Kumar is a speaker for Janssen Pharmaceuticals and Novo Nordisk A/S. She is a shareholder in Zafgen, VIVUS, and MYOS Corporation. L.J. Aronne has received research funding from Aspire Bariatrics, Eisai, and Takeda Pharmaceuticals. He declares consultant/advisory board work with Jamieson Labs, Pfizer Inc, Novo Nordisk A/S, Eisai, VIVUS, GI Dynamics, JOVIA Health, and Gelesis. He is a shareholder of Zafgen, Gelesis, MYOS Corporation, and Jamieson Labs, and he is on the board of directors of MYOS Corporation and Jamieson Labs.

Comprehensive Weight Control Center, Division of Endocrinology, Diabetes, and Metabolism, Weill Cornell Medicine, 1165 York Avenue, New York, NY 10065, USA
* Corresponding author.
E-mail address: kph2001@med.cornell.edu

Med Clin N Am 102 (2018) 135–148
https://doi.org/10.1016/j.mcna.2017.08.010 **medical.theclinics.com**

expenditure are counteracted by adaptive physiologic responses.[2] Not only does appetite increase but resting metabolic rate slows out of proportion to what would be expected based on changes in body composition.[3] This phenomenon, called adaptive thermogenesis or metabolic adaptation, impedes weight loss and contributes to weight regain.[4,5]

Antiobesity pharmacotherapy is one strategy to offset the adaptive changes in appetite and energy expenditure that occur with weight loss and to improve adherence to lifestyle interventions.[3] According to the 2013 American College of Cardiology/American Heart Association/The Obesity Society's guideline for the management of overweight and obesity in adults and the Endocrine Society's clinical practice guidelines on the pharmacologic management of obesity, pharmacotherapy for obesity can be considered if patients have a body mass index (BMI) of 30 kg/m^2 or greater or a BMI of 27 kg/m^2 or greater with weight-related comorbidities, such as hypertension, dyslipidemia, type 2 diabetes, and obstructive sleep apnea.[1,6]

As obesity is a chronic disease, most antiobesity medications are approved for long-term treatment. Until a few years ago, phentermine (and other sympathomimetic amines) and orlistat were the only antiobesity medications approved by the Food and Drug Administration (FDA). In 2012, phentermine/topiramate extended release (ER) and lorcaserin were approved; in 2014, naltrexone sustained release (SR)/bupropion SR and liraglutide 3.0 mg were approved.

In this article, the authors review the 6 most widely used antiobesity medications (**Table 1**). The authors present efficacy and safety findings, discuss how to best select agents for each patient, and provide advice on how to manage patients who do not respond to medications. Although referral to an obesity medicine specialist is an option for some primary care providers, there are not enough obesity medicine specialists to address the obesity epidemic. Therefore, it is important for primary care providers to be familiar with the pharmacotherapy available to patients who are unable to lose weight and sustain weight loss with lifestyle interventions alone.

PHENTERMINE

Phentermine was approved by the FDA in 1959 and has been the most commonly prescribed medication for obesity in the United States. It is an adrenergic agonist that increases resting energy expenditure and suppresses appetite. Phentermine is indicated for short-term use (3 months), as there are no long-term safety trials of phentermine monotherapy; but it was approved in combination with topiramate ER for long-term therapy. Many practitioners prescribe phentermine for greater than 3 months as off-label therapy for ongoing weight management.

Two other sympathomimetic amines, diethylpropion and phendimetrazine, are also available in the United States; but data on these agents are minimal, and they are prescribed much less frequently.

Until recently, the available doses of phentermine were 15.0, 30.0, and 37.5 mg.[7–9] As prescribing practices should be individualized to determine the lowest effective dose, many practitioners recommend using quarter or half tablets of these formulations. In 2016, the FDA approved an 8-mg formulation, which can be prescribed up to 3 times daily.[10] Administration of the last dose late in the day should be avoided to prevent insomnia. Phentermine is a schedule IV controlled substance.

In a 28-week randomized controlled trial comparing phentermine, topiramate ER, and the combination of the two agents, phentermine 15 mg daily produced an average 6.0-kg weight loss compared with a 1.5-kg weight loss with placebo.[11] Forty-six percent of participants assigned to phentermine lost at least 5% of initial body weight