

should be preceded by a warm-up period to minimize injuries.

Long-term lifestyle modification trials, such as the Diabetes Prevention Program, have targeted 150 minutes of exercise per week. Newer guidelines recommend 60 to 90 minutes of daily exercise, with a minimum of 150 to 175 minutes per week needed to obtain weight loss benefit. Emphasis should be placed on moderate-intensity exercise, such as walking 20-minute miles, rather than strenuous exercise. Because patients who are not used to exercising may find it difficult to incorporate physical activity into daily practice, it is also important to use a variety of exercises to maintain interest. Increasing exercise duration to 300 minutes/week was found to help in long-term maintenance of weight reduction. Frequent short bouts of exercise as brief as 10 minutes each can increase adherence to a regimen.

Behavior Modification and Patient Education

Cognitive-behavioral intervention and patient education are important components of successful weight loss programs. Whenever possible, cognitive-behavioral intervention should be conducted by an experienced psychologist. The fundamental principles of intervention typically include behavioral goal setting, stimulus control techniques, cognitive restructuring, assertive communication skills, stress management, and relapse prevention. Cognitive-behavioral support conducted in a group setting with weekly meetings is frequently successful. Patients should learn how to set *SMART* goals (*s*pecific, *m*easurable, *a*ction-oriented, *r*ealistic, *t*ime-limited). It can be helpful to emphasize real-life examples (e.g., success stories, logbook learning, recommitting to progress). The behavioral modification strategy should assist patients in identifying precipitants for deviations from a diet (e.g., timing, types of food or exercise, situations, feelings), overcoming challenges (planning ahead, delay and distraction, problem solving), managing automatic negative thinking (“detour thoughts”), coping with cravings through mindful strategic eating, preventing relapses using logbook learning, navigating social eating, and setting personal weight maintenance plans.

Pharmacologic Options

The four anti-obesity drugs currently licensed for use in the United States are orlistat, phentermine, lorcaserin, and the combination of phentermine and long-acting topiramate. Except for phentermine by itself, the three other medications are approved for long-term management of obesity.

Orlistat

Orlistat limits caloric intake through inhibition of the lipase-mediated breakdown of fat in the gastrointestinal tract. This mechanism results in an approximately 30% reduction of fat absorption and an increase in fecal fat content. In addition to weight loss, orlistat use has been associated with decreased incidence of diabetes, improved concentrations of total cholesterol and low-density lipoprotein (LDL)-cholesterol, and improved blood pressure and glycemic control in patients with diabetes. However, high-density lipoprotein (HDL)-cholesterol has been found to be slightly lowered. Most people develop side effects with variable degrees of diarrhea, flatulence, oily stools, fecal

urgency, and, rarely, fecal incontinence. There also is an increased risk of cholelithiasis. Gastrointestinal side events are usually proportional to the amount of fat intake. Supplemental fat-soluble vitamins A, D, E, and K must be taken to prevent possible deficiencies. The usual dose of orlistat is 120 mg before each meal. A 60 mg dose formulation is currently available over the counter; it is less effective but is also associated with fewer side effects.

Phentermine

Phentermine is approved for short-term treatment of obesity (up to 6 months). Because phentermine has actions similar to amphetamines, it can elevate blood pressure, increase heart rate, and stimulate the central nervous system (frequently causing insomnia), in addition to suppressing the appetite. The recommended phentermine dose is 30 mg once daily. Combining phentermine with tricyclic antidepressants or monoamine oxidase inhibitors may result in substantial increases in blood pressure and other serious reactions because of elevated serotonin levels in the blood.

Lorcaserin

Lorcaserin is a selective serotonin (5-hydroxytryptamine) receptor agonist with specificity for the 5-HT_{2C} receptor subtype. The activation of these receptors in the hypothalamus is thought to activate production of proopiomelanocortin (POMC) and, consequently, to promote weight loss through satiety signals. Lorcaserin has 100-fold higher selectivity for 5-HT_{2C} versus the closely related 5-HT_{2B} receptor. Activation of the 5-HT_{2B} receptor by the less selective agents fenfluramine and dexfenfluramine previously was linked to serious cardiac valvulopathy, but there is no evidence for this adverse effect with lorcaserin. Clinical trials showed that 47.5% of patients treated with lorcaserin lost at least 5% of their initial body weight, and 22.6% lost at least 10%, in 1 year. Lorcaserin treatment also resulted in significantly lower glycosylated hemoglobin (HbA_{1c}) values in patients with T2DM and improved lipid profile and decreased blood pressure in clinical studies.

Lorcaserin is approved for use as an adjunct to a reduced-calorie diet and exercise for chronic weight management in patients with initial BMI values of 30 kg/m² or higher and in those with BMI values of 27 kg/m² or higher with at least one weight-related comorbid condition (e.g., hypertension, dyslipidemia, T2DM). It is given in a dose of 10 mg twice daily. Side effects usually are mild to moderate, with the most common being headache, upper respiratory tract infection, nasopharyngitis, sinusitis, dizziness, nausea, and fatigue. The U.S. Drug Enforcement Administration has classified lorcaserin as a schedule IV drug because it has hallucinogenic properties that could lead to psychiatric complications.

Phentermine and Long-Acting Topiramate

Phentermine is an appetite suppressant and stimulant of the amphetamine and phenethylamine class (see earlier discussion for details on the use of phentermine alone for weight reduction). Topiramate is an anticonvulsant that was found to have weight loss side effects. The combination of phentermine plus low doses of topiramate has been shown to have synergistic effects on weight loss. As with lorcaserin, this combination tablet is

