

# Bariatric Rehab

What you should know about the new drug therapies.

BY MARIANNE WINFIELD

Therapists have gained two new tools in their work with bariatric patients — two drugs have been approved this year for use as anti-obesity medications and are increasingly being incorporated into rehab regimens.

What should rehab professionals know about these new therapies?

According to the American Society of Bariatric Physicians, most available weight-loss drugs affect the body's nervous system by suppressing appetite and possibly altering the way the body burns calories.

Two of the newer drugs that show promise in the fight against obesity differ in this respect. Orlistat (Xenical) is a non-systemic fat blocker; bupropion (Wellbutrin, Zyban) seems to make patients feel rewarded much quicker than they would without the drug.

While orlistat has been approved for weight loss and maintenance by the Federal Drug Administration, bupropion is still

indicated only for depression (Wellbutrin) and smoking cessation (Zyban).

Bupropion is unrelated to selective serotonin reuptake inhibitors or tricyclic antidepressants, which can increase blood pressure. As an antidepressant that acts only on dopamine and norepinephrine, it is in a class by itself.

Donald Robertson, MD, MSc, medical director of the Southwest Bariatric



Nutrition Center in Scottsdale, Ariz., sees orlistat as the “forerunner in an explosion in similar drugs that will be used in combination with central nervous system-acting drugs like bupropion.”

Describing orlistat as a whole new class of drug, Robertson adds, “It can be useful on a PRN basis; that is, you take one when you know you will be having a high-fat meal. But it has unpleasant GI side effects. And at three times a day, it’s not a cheap drug. Its main place is probably going to be in long-term maintenance.” Orlistat costs around \$100 per month.

“Obviously, we hate to see a 30-year-old on medication, so we try to do everything in our power to avoid it,” says Lisa Nicholson, PhD, RD, a specialist in health behavior research at the University of Southern California School of Medicine. “But at a certain point, drugs can be useful and appropriate. When a person’s weight is very high, it’s not always a question of weakness of willpower. We don’t blame a Type-I diabetic or a schizophrenic for needing medication. It’s the same with cholesterol-lowering drugs.

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"In the future, there will be additions to the class of drugs that interact on a hormonal basis," she added. "There will be more drugs like leptin."

Currently being studied in human clinical trials, leptin is the protein produced in fat cells. An editorial in the *New England Journal of Medicine* (NEJM 1996; 334:324-325) describes leptin as a "satiety signal in a feedback loop" thought to affect appetite and satiety centers of the

brain. It drew "strong positive correlation" between serum leptin concentrations and the percentage of body fat, the body-mass index, and basal serum insulin concentrations.

As Robertson told *Rehab Report*, "leptin is the key to unraveling the cause and treatment of obesity."

In the meantime, however, the appearance of drugs such as orlistat and bupropion show promise.

## 'A Whole New Class of Drug'

Orlistat (Xenical), manufactured by Basel, Switzerland-based Hoffman-La Roche, was approved by the FDA in April 1999 as the only prescription lipase inhibitor.

Lipase is an enzyme in the gastrointestinal tract that breaks down dietary fat molecules into pieces small enough for the body to absorb and store. When orlistat inactivates lipase, up to one-third of dietary fat cannot be hydrolyzed and passes undigested through the body. Two-thirds of ingested fat is absorbed normally.

Because metabolism takes place mainly within the gastrointestinal wall, systemic exposure to orlistat is minimal. Its estimated half-life is one to two hours, and it is mainly eliminated by fecal excretion.

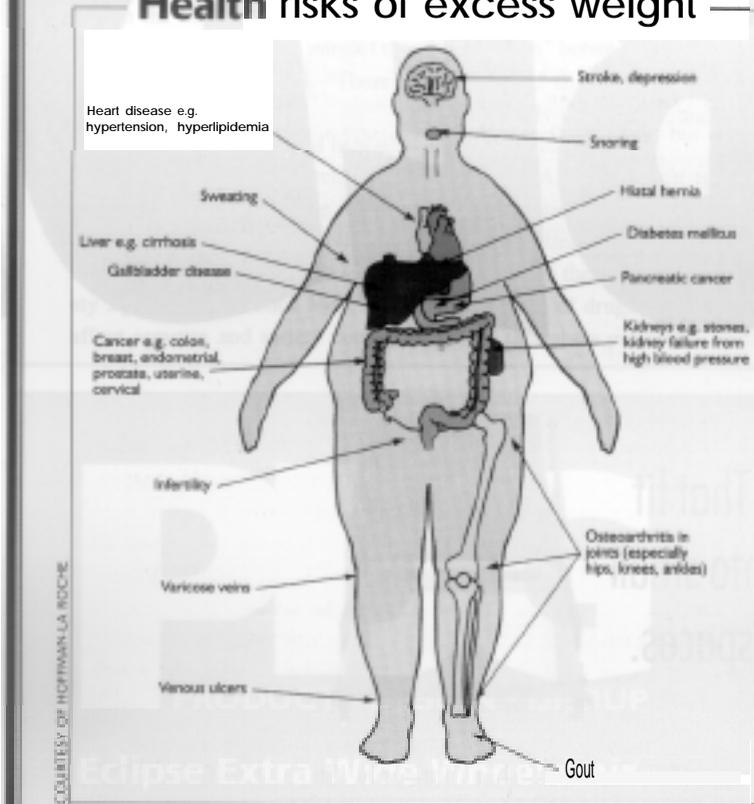
Orlistat is indicated when a patient has an initial body-mass index of  $\geq 30$ . But with obesity-related risk factors such as hypertension, dyslipidemia and diabetes, the BMI drops to  $\geq 27$ .

In conjunction with a reduced-calorie diet, it is indicated for weight loss, maintenance and reducing the risk of regain after weight loss. Contraindicated in patients with chronic malabsorption syndrome or cholestasis, it carries a warning to exclude organic causes of obesity such as hypothyroidism.

As a precaution, patients are advised to adhere to a nutritionally balanced, reduced-calorie diet containing no more than 30 percent of calories from fat. In addition, because orlistat has been shown to inhibit the absorption of vitamins A, D, E (up to 60 percent) and K, and beta-carotene, patients should take a multivitamin supplement containing fat-soluble vitamins at least two hours before or after administration.



## Health risks of excess weight



Pooled data from two-year clinical studies of patients taking orlistat vs. placebo — both on reduced-calorie diets — indicate that almost three times as many patients taking orlistat achieved weight loss of more than 10 percent body weight. Twice as many lost at least 5 percent body weight.

In addition, patients taking orlistat lost more than 60 percent more weight than those on the reduced-calorie diet alone, with improved metabolic, cardiovascular and anthropometric measurements. The most common adverse effects were gastrointestinal, and those generally subsided after the first year, according to Hoffmann-LaRoche.

The drug maker offers a tailored educational program and diet support system called XeniCare. A starter kit includes an explanation booklet, questionnaire, wellness contract, daily journal and nutritional reference card. After registering for the program, the patient receives another kit by mail followed by personalized mailings and quarterly support newsletters.

## An Antidepressant 'Like No Other'

Duke University researchers monitoring patients being treated with bupropion for depression noticed a side-effect of weight loss. Those observations led to studies in non-depressed obese patients. Also indicated for smoking cessation, bupropion (Zyban), is an aminoketone manufactured by Greenford, England-based Glaxo Wellcome.



It is chemically unrelated to other known antidepressant agents, and unlike most of the newer ones, has weaker effects on serotonin reuptake. Bupropion acts on noradrenergic and dopaminergic sites in the brain that are implicated in sensations of reward and pleasure. However, the exact mechanism by which it functions as an antidepressant is not known.

Results of a pilot study at Duke University show that women who took 400 mg/day of bupropion SR, combined with a reduced-calorie diet, lost four times more weight than women on a placebo plus diet. Data are still being collected on the effects of bupropion on bone density and lean muscle mass.

In the original clinical studies of bupropion for use as an antidepressant — performed by Hoffmann-LaRoche for the FDA — patients receiving tricyclic antidepressants gained four times more weight than patients on the immediate-release formulation of bupropion. However, TCAs are well-known to cause weight gain.

People given the maximum recommended dose of 400 mg/day of bupropion SR were three times more likely than those taking a placebo to lose more than 5 pounds. At 400 mg/day, the most common adverse effects were dry mouth (24 percent), nausea (18 percent) and insomnia (16 percent), according to results from the manufacturer's FDA studies.

Bupropion has several contraindications, including patients with renal dysfunction, seizure disorders or eating disorders.

## A Multi-Faceted Approach to Obesity Treatment

“The problem of obesity is an ongoing issue,” says Joy Hammel, PhD, OTR/L, FAOTA, an assistant professor in the occupational therapy department at the University of Illinois, Chicago. “So many obese people don’t come in for treatment until they have developed really serious life-threatening conditions.”

According to Donald Robertson, MD, MSc, medical director of the Southwest Bariatric Nutrition Center in Scottsdale, Ariz., a major culprit is “visceral fat” – the kind stored deep in the liver, pancreas, colon and intestines.

More serious than subcutaneous fat, it is thought to disturb carbohydrate and cholesterol metabolism and has been linked to insulin resistance. Even minimal weight loss (5 percent to 10 percent) can significantly improve blood pressure, blood sugar, cholesterol, triglycerides and low-density lipoproteins (LDLs).

“Obesity is not a character flaw. It’s a medical condition, part genetic, part environmental. It has very little to do with willpower, sloth or lack of control,” said Robertson. “It can be described as ancient genes in conflict with modern lifestyles. We used to have to catch our food, and it wasn’t there every day. So we developed a genetic propensity to store fat – big time. Fat is the body’s way of anticipating bad times.”

Robertson points to recent studies (*Drug Therapy*, Sept. 1993:17-29) that show that the most successful multimodal pro-

grams for long-term weight loss and maintenance include a drug component. “While exercise is obviously very effective when used together with diet, obese patients often have major limitations on what they can do physically,” said Robertson. “You don’t put a 400-lb. person on a jogging program.”

“It’s important to treat the person, rather than the condition,” observes Lisa Nicholson, PhD, RD, who specializes in health behavior research at the University of Southern California School of Medicine.

“A variety of courses may be followed, depending on the philosophy of the location and the etiology of the disease, from surgical stapling to ultra-low-calorie fasting.”

“Obesity is a multifaceted disease. We have to stop treating obesity with a cookie-cutter approach,” says Nicholson. “What we should be doing is following the 5 percent of patients who have kept at least 100 pounds off. They all begin by really looking at their own lives, individualizing lifestyle approaches to healthy ways of achieving emotional and psychological satisfaction. The moment you impose a regimen on yourself that is not comfortable for you, the more you are going to rebel against it.” 

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