

# Intensive Lifestyle Intervention Delivers a Bonanza of Benefits

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MUNICH — Obese type 2 diabetes patients with metabolic syndrome saw dramatic improvements in cardiac function and multiple cardiovascular risk factors after only 3 weeks in a German pilot study of an intensive lifestyle modification program including aerobic exercise and a low glycemic and insulinemic diet.

The catch? Those first 3 weeks of lifestyle modification were conducted on an inpatient basis. That's essential to the program's success because it enables patients to see the kind of early impressive benefits that result in greater buy-in and improved long-term adherence, Dr. Helene von Bibra said at the annual congress of the European Society of Cardiology.

She presented the results of an innovative prospective study involving 25 patients with type 2 diabetes and metabolic syndrome. Their baseline mean body mass index was 37 kg/m<sup>2</sup>, with 41% body fat. They averaged 52 years of age and had a 4-year history of diabetes. None of the participants had known coronary disease. Nineteen were on oral antidiabetic medications.

The inpatient intervention included 2 hours of supervised moderate-intensity aerobic exercise daily and a low glycemic and insulinemic (LOGI) diet developed by Dr. David S. Ludwig, director of the obesity program at Children's Hospital Boston, and a pediatric endocrinologist at Harvard Medical School, Boston.

This low-carbohydrate diet derives 30% of calories from protein, 45% from fat, and only 25% from carbohydrate. The LOGI food pyramid described by Dr. Ludwig features unlimited consumption of fruits and most vegetables at its base. The second layer consists of low-fat dairy products, eggs, fish, lean meats, nuts, and legumes. Next come whole grains and pasta. The small peak of the pyramid comprises refined flour, potatoes, and desserts.

It's a diet designed to reduce postprandial blood glucose peaks and compensatory hyperinsulinemia while lowering blood pressure and improving lipid abnormalities, explained Dr. von Bibra of Bogenhausen Academic Hospital and State Clinic, Munich.

The LOGI diet was adopted for the program because of mounting evidence that traditional "heart healthy" low-fat diets are of questionable effectiveness. Dr. von Bibra cited a recent article by Dr. Paul R. Marantz and colleagues at Albert Einstein College of Medicine in New York that has been influential in Germany. The authors argue that U.S. national dietary guidelines introduced in the late 1970s that advocated low-fat diets for public health reasons were based on weak scientific evidence. Moreover, encouraging low-fat diets may have had the unintended consequence of contributing to the worsening obesity epidemic by leading to overconsumption of carbohydrates, according to Dr. Marantz and his coauthors (*Am. J. Prev. Med.* 2008;34:234-40).

Dr. von Bibra reported that after 3

weeks of inpatient lifestyle modification, patients showed mean reductions of 2.6 kg in body weight, 3.7 cm in waist circumference, 54% in postmeal insulin, and 6 mm Hg and 5 mm Hg in systolic and diastolic blood pressure, respectively. Of 19 patients initially on antidiabetic drugs, 13 were no longer taking them after 3 weeks; the remaining 6 patients were all taking lower doses.

The study was underwritten by a large health care and pension fund. ■

## Key Metabolic and Cardiac Function Changes After Intensive Lifestyle Intervention

	Baseline	At 3 Weeks
Body mass index	37 kg/m <sup>2</sup>	36.1 kg/m <sup>2</sup>
Waist circumference	123 cm	119.3 cm
Triglycerides	192 mg/dL	145 mg/dL
Total cholesterol	207 mg/dL	195 mg/dL
HbA <sub>1c</sub>	7.0%	6.7%
Fasting blood glucose	147 mg/dL	130 mg/dL
Postmeal glucose	143 mg/dL	123 mg/dL
High-sensitivity C-reactive protein	5.8 mg/L	3.8 mg/L
Systolic myocardial velocity	7.5 cm/sec	7.9 cm/sec
Diastolic myocardial velocity	9.6 cm/sec	10.5 cm/sec

Source: Dr. von Bibra

ELSEVIER GLOBAL MEDICAL NEWS

## IMPORTANT CORRECTION OF DRUG INFORMATION ABOUT EFFEXOR XR® (VENLAFAXINE HCl) EXTENDED-RELEASE CAPSULES

An advertisement in professional journal publications for EFFEXOR XR® (venlafaxine HCl) Extended-Release Capsules for the treatment of major depressive disorder was the subject of a Warning Letter issued by the U.S. Food and Drug Administration (FDA) in December 2007. The FDA stated that the journal ad was misleading because it overstated the efficacy of EFFEXOR XR, made unsubstantiated superiority claims, and contained other unsubstantiated claims regarding EFFEXOR XR.

Wyeth would like to take this opportunity to clarify the content of the advertisement.

### Claims that Reference the Baldomero et al Study and Other Related Claims

The FDA objected to the claim, "In an open-label study of patients who failed previous antidepressant treatment, nearly 60% achieved remission when changed to EFFEXOR XR." The FDA determined that the Baldomero study (the cited reference for this claim) could not be relied upon as substantial evidence to support the claim due to the following reasons: (1) the study was an open-label study, which is not an appropriate study design to measure subjective end points because it fails to minimize potential bias; (2) the study did not include a placebo group, so there was no way to determine the actual effect size of the drug; and (3) the study did not provide information about whether EFFEXOR XR was superior to failed therapy because study subjects were not randomized to their previously failed therapy. Therefore, the FDA stated that the study failed to support the 60% remission rate claim as well as any conclusion that EFFEXOR XR is superior to other antidepressant treatments. In addition to the above claim, the FDA stated that other claims added to the misleading impression that patients who have failed previous antidepressant therapy can expect improvement when switching to EFFEXOR XR.

### Claims from the PREVENT Study

The FDA objected to the claim, "In the PREVENT study, the probability of preventing a new episode of depression was 92% with EFFEXOR XR in maintenance year 2 vs. 55% with placebo." The FDA stated that the cited claim overstated the efficacy of EFFEXOR XR by implying that the general patient population suffering from major depressive disorder can expect a 92% probability of preventing a recurrent depressive episode after two years of treatment when this is not supported by substantial evidence.

The cited study for this claim was a randomized, multicenter, double-blind study (n=1096) comparing EFFEXOR XR with placebo. The study was designed to provide efficacy data regarding recurrence prevention with EFFEXOR XR after two years of maintenance

treatment. It followed patients through 4 different time periods: a 10-week acute period, a 6-month continuation period, an initial 12-month maintenance period (maintenance year 1), and a second 12-month maintenance period (maintenance year 2). At the end of each period, patients were only considered eligible for inclusion in the next period if they were still responding to the drug. Patients dropped out of the study during each of the periods for different reasons (eg, lack of efficacy, adverse events). At the start of each maintenance period, the remaining patients who still showed a response to EFFEXOR XR were re-randomized to EFFEXOR XR or placebo. Because a high percentage of EFFEXOR XR patients were either re-randomized to placebo or were discontinued from the study before entering maintenance year 2 and because only patients who responded to EFFEXOR XR were selected to continue to the next phase of treatment, the FDA determined that the results of the study could not be extrapolated to the general patient population suffering from major depressive disorder.

### Claim Regarding Clinical Experience and Number of Patients

The FDA objected to the claim, "More than 12 years of clinical experience and over 20 million patients treated with EFFEXOR/EFFEXOR XR." The claim of 20 million EFFEXOR/EFFEXOR XR patients was estimated from the number of U.S. prescriptions, average daily consumption, and average length of therapy. The FDA determined that this claim was misleading based on the referenced data because the calculations used did not reflect the number of "unique" patients. Because there are no unique patient-level data available for the entire 14-year period during which EFFEXOR/EFFEXOR XR has been on the U.S. market, the claim is no longer used in EFFEXOR XR promotional materials.

### Please see brief summary of Prescribing Information on adjacent page.

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