Weight loss 'electroceutical' device wins FDA okay

In January, St. Paul, Minnesota–based EnteroMedics received the US Food and Drug Administration's (FDA) go-ahead to market its Maestro Rechargeable system. This surgically implanted device, which targets the vagal nerve pathway, is the first weight-loss device approved in the US since 2007. EnteroMedics now gains entry into the lucrative, yet underserved, surgical weight-loss market. Currently, surgical solutions serve only about 2.5% of the morbidly obese population in the US, a $1.2-billion market in 2013. But this could grow to $3 billion by 2030, estimates William Plovanic, a medical device analyst at Vancouver, British Columbia–based Canaccord Genuity, judging by the raft of minimally invasive weight-loss procedures currently in the pipeline.

The agency approved EnteroMedics' device for treating adults with morbid obesity—a body mass index (BMI) of at least 40–45 kg/m^2 or a BMI of at least 35–39.9 kg/m^2 for those with an obesity-related condition such as type 2 diabetes. The Maestro Rechargeable System is a pacemaker-like device implanted under the abdominal skin and connected by electrical leads to the vagal nerve. It delivers what the company terms VBLOC therapy: intermittent electrical pulses delivered during a person's waking hours to block vagus nerve activity.

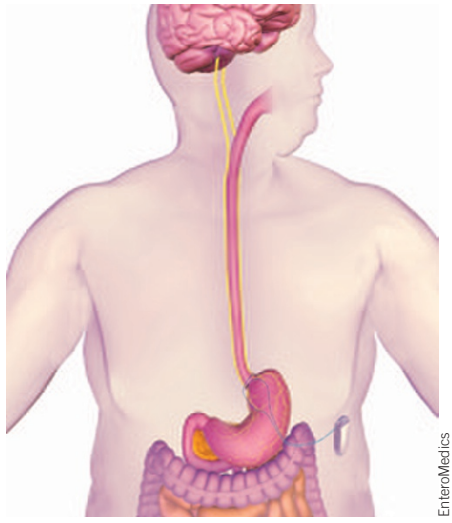
The vagus nerve is a major conduit between brain and gut, and in addition to affecting hunger, it also influences gastric relaxation, levels of stomach acid and appetite-regulating hormones such as ghrelin. Patients with VBLOC report they are no longer "driven to look for food all of the time," says Mark Knudson, EnteroMedics CEO.

The exact mechanisms underpinning weight loss with this neurodevice are unknown. But Knudson says the device's utility is backed by almost 40 years' experience with vagotomies. This practice of cutting the vagus nerve to treat peptic ulcers became obsolete during the 1980s, although a commonly observed side effect from the procedure was weight loss.

To test VBLOC therapy, EnteroMedics ran a sham-controlled study, in which the device was implanted with no leads (the sham study was the first of its kind for a medical device). At 12 months, results from 239 patients fell short of the predefined 10% weight reduction needed for approval. The 162 treated patients lost an average of 24.4% excess body weight compared with an average 15.9% reduction in the 77-patient sham group. At 18 months, 117 treated patients out of a total of 159 maintained the initial weight loss compared with 42 patients in the sham group who maintained a loss of only 12% excess weight. Only 4.3% of patients experienced any severe side effects. Based on these results, the agency approved the device, citing efficacy over time and safety.

Surgical procedures to treat obesity—gastric banding and gastric bypass—are effective but extremely underused. Last year, fewer than 180,000 surgical weight-loss procedures were performed—only about 0.3% of the total, addressable, obese-patient population, which includes patients with BMIs under 35 kg/m^2 who don't qualify for surgery. Even patients eligible for surgery are often turned off by the potential complications, which have been reported to be as high as 40%, and the risk of side effects that include micronutrient deficiencies, vomiting, cramping, nausea and diarrhea. Most of the new devices or procedural interventions in the pipeline are reversible and minimally invasive, which is a huge selling point, says Plovanic. Given the unmet need and the low uptake of existing interventions, "the market is poised for significant growth."

VBLOC's approval adds another option to a growing list of strategies to combat obesity, but all have their drawbacks, says Stephen Bloom, head of diabetes, endocrinology and metabolism at Imperial College, London. Bloom is currently in the preclinical stages of testing a weight loss device that also modulates the vagus nerve, funded by a €7 ($7.9)-million European research grant. For EnteroMedics' device, it will be important to ascertain whether weight loss can be sustained long term, as the nervous system is adaptive, and nerves may reroute to compensate for the disrupted vagal signaling, Bloom says. Given that the vagus nerve also influences heart rate and respiratory function, other side effects, some severe, may turn up over time. The FDA is requiring EnteroMedics to track at least 100 patients for five years after Maestro comes on the market.



The Maestro device sits under the abdominal skin and connects by electrical leads to the vagal nerve.

Another device similar to VBLOC to treat obesity-induced diabetes developed by Dusseldorf, Germany–based MetaCure entered the European market in 2006. The device stimulates the stomach muscles before meals to induce feelings of satiety to prevent overeating. Fewer than 200 people have received implants, however, and clinical studies to date have been small, with only two to four years follow-up. Still in preclinical development is Caesarea, Israel–based Beta-Sim's device, which electrically stimulates the beginning of the small intestine to delay gastric emptying.

Several other weight loss devices, which work by different mechanisms, are in the pipeline; three have already been submitted to the FDA, and another five are in clinical trials. These include balloon fillers that expand after being swallowed to limit food intake, devices that manipulate the rate at which food exits the stomach, and devices that cause food to be poorly absorbed or to bypass the intestines entirely.

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Correction

In the December 2014 issue, the article "Celgene wagers on Sutro's cell-free platform to ramp up ADCs" incorrectly specified "ADCs" in the title, rather than "bispecifics." The error has been corrected in the HTML and PDF versions of the article.

In the January 2015 issue, in the article "Foundation receives $3.3-billion windfall for Kalydeco," Howard Fillit's affiliation was given as the Alzheimer's Disease Research Foundation instead of the Alzheimer's Drug Discovery Foundation. The error has been corrected in the HTML and PDF versions of the article.