Rival obesity drugs seek out patients, and acceptance

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Between 1999 and 2012, the Food and Drug Administration gave its blessing to exactly zero new weight-loss drugs. Then, starting in June of last year, the agency approved two such medications, in a span of 20 days.

The FDA didn't become a giddy cheerleader overnight. In fact, both drugs - Belviq, by Arena Pharmaceuticals Inc., and Qsymia, by Vivus Inc. - underwent a torturous path to approval because of concerns about their safety or effectiveness.

The drugs' approval is a statement on the nationwide epidemic of obesity more than anything else. More than one-third of American adults are obese. The FDA essentially acknowledged that, for a certain segment of the population, the remedies at hand - diet, exercise and, in extreme cases, bariatric surgery - aren't working.

"Obesity is such a huge problem, because it leads to so many other problems: coronary disease, arthritis, diabetes, depression," said Dr. Rajesh Gulati, a clinical professor at UC Irvine's School of Medicine, and the medical director at the university's Weight Management Program. "Our health-care bills are going through the roof. If somebody is able to produce that magic pill, that guy is going to turn into a billionaire overnight.

"That is the motivating thing that keeps these companies producing these drugs."

Neither Belviq nor Qsymia is a magic pill. In fact, both have potential side effects severe enough that the FDA initially rejected them. The drugs are intended not for people who simply want to lose a few pounds but for those who meet the threshold of obesity: a body-mass index of at least 30 (a person who is 6 feet tall and weighs 221 pounds has a BMI of 30), or a BMI of at least 27, along with another weight-related problem such as high blood pressure, high cholesterol or type 2 diabetes. The drugs are meant to be used in conjunction with lifestyle changes, like healthful eating and exercising.

But clinical trials have shown they're effective at helping people lose weight. The trick is convincing skeptical physicians, and patients, that they work well enough, and that they're safe enough, for long-term use.

CHECKERED HISTORY

Weight-loss aids have been around for generations, and in the 1950s, amphetamines became the rage because they sped up metabolism and produced weight loss. They also caused heart problems and created addicts.

In 1973, the FDA-approved drug fenfluramine was introduced in the United States and sold under the brand names Pondimin, Ponderax and Adifax. The drug increased the level of serotonin, a feel-good chemical in the body, producing a sensation of fullness. The initial problem was the effects didn't last. In the 1990s, the drug company American Home Products (which later became Wyeth) combined fenfluramine with phentermine, an appetite suppressant, and a new product, fen-phen, was born.

Fen-phen was the hot weight-loss drug of the day, and thousands of people shed pounds with it. But gradually, reports started coming in about elevated hypertension readings, then damage to heart valves. In a

much-publicized case, Mary J. Linnen, 30, of Quincy, Mass., became ill only 24 days after taking fen-phen in the spring of 1996. She had been trying to lose weight so she could fit into just the right wedding dress. She died of heart problems on Feb. 22, 1997.

The drug was pulled from the market in September 1997, and the company settled thousands of lawsuits for $3.75 billion.

Others have come and gone: Sibutramine, marketed as Meridia, was withdrawn in 2010 because of high incidence of cardiovascular problems and strokes. Orlistat, marketed as Xenical (and in an over-the-counter version called Alli), was the last weight-loss drug approved by the FDA before the two new ones. It works in a different way, blocking the absorption of fats. But its distasteful side effects, including oily stools, make it unpalatable to many users.

ABOUT BELVIQ

Belviq (pronounced bell-VEEK), whose chemical name is lorcaserin, is made by San Diego-based Arena Pharmaceuticals and marketed by Japan's Eisai Inc. It was approved by the FDA on June 27, 2012, but an agency advisory panel had rejected it in 2010 because of safety concerns.

The most common side effect is headache, which occurred in about 18 percent of patients in clinical trials, compared to 11 percent with a placebo. But a larger concern is the same kind of heart-valve problems that plagued fenfluramine. The drug also could cause hallucinations if taken in higher dosages than prescribed.

The federal Drug Enforcement Agency classified the drug as a Schedule IV controlled substance, same as Qsymia. That means there's only a slight risk of abuse. But the concern over the drug's "hallucinogenic

properties" delayed it getting to market, and it became available to the public only earlier this month.

How does Belviq work? It turns on a specific receptor that's normally stimulated by serotonin, bringing the sensation of satiety.

"The way we went about it is the recognition that serotonin is a very important hormonal system, one of the few mechanisms that can overcome this drive," said Dominic Behan, co-founder of Arena and the company's chief scientific officer. "The challenge is, there are many serotonin receptors: one we wanted to target, and we wanted to avoid the others, because if we stimulated them we'd run into side effects."

How well does it work? According to clinical trials, 47 percent of patients on the medication lost at least 5 percent of their body weight during the course of one to two years, compared with 23 percent of those on a placebo.

ABOUT QSYMIA

Qsymia (pronounced cue-SIMM-ee-uh) is a combination of phentermine, the safer "phen" component of fen-phen, and topiramate, an anti-seizure medication that also promotes weight loss. It's made by Mountain View-based Vivus.

Qsymia was approved by the FDA on July 17, 2012, three weeks after Belviq. But Qsymia got the jump on its rival because Belviq was subjected to the DEA's scheduling process. The head start didn't help Qsymia much, though, because it was slow to gain traction among physicians, and because insurers were reluctant to pay for it.

Since its September launch, Qsymia has cleared several hurdles: After a regulatory evaluation period, next month it will start being sold by

pharmaceutical retailers; currently it's available only through mail-order. It's also prescribed in the Veterans Affairs system. And now 34 percent of private insurance policies cover it.

How does it work? The two drugs acting together suppress appetite, and since the separate components have been prescribed previously, it's a known commodity for physicians.

"Individually, we have years of data on them. That's always key in terms of the comfort level," said Dr. Christian Gastelum, an endocrinologist who treats obese patients in East Los Angeles and Whittier, Calif.

How well does it work? According to clinical-trial data, 70 percent of people taking it lost at least 5 percent of body weight, compared with only 20 percent on a placebo.

COMPARISONS

Although pregnant women should not take either drug, there's a particular danger of birth defects with Qsymia, which is part of the reason the FDA initially rejected it, in 2010 (back then it was called Qnexa; the FDA asked for the name to be changed to avoid confusion with other, similar-sounding branded drugs).

Vivus says women of child-bearing age must use contraception while on the drug, and should take a pregnancy test once a month while on it.

Meg Evans of Spring Valley, east of San Diego, says Qsymia has helped her.

She's 64, a former basketball player at Gonzaga University, and has struggled for years with her weight since giving birth to four daughters, now grown. At 5 feet 7, she weighed 230 pounds when she took part in

Qnexa trials in 2008, and she lost 50 pounds. Once the trial ended, she gained back 20 pounds. But since she began taking Qsymia in January, she's lost 17 pounds.

"I fully believe diet and exercise are major factors," she said. "The Qsymia helps me stem my appetite, but it's not a magic bullet. I'm pretty sure I could take the Qsymia and still not lose any weight if I didn't watch what I eat and exercise."

Gulati, of the UCI School of Medicine, said he expects consumers to "make a beeline" for both drugs.

"People are fed up with weight, they'd like to lose weight, they've tried their best, and they're not succeeding," he said.

But he said the way the drugs work, interacting with the "normal metabolism of the body," is troubling. He says 5 percent weight loss, "in the grand scheme of things, is nothing."

Then there's that famously sketchy historical track record of weight-loss drugs.

"Fen-phen came out huge, then the side effects came in," he said. "I'm not saying every research is cooked up, but that's a lot of money companies are spending."

Also, he said: "These drugs have not been tested long enough on populations that are extremely sick, and that is a problem."

WEIGHING THE OPTIONS

Belviq

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Pronounced: bell-VEEK

Approved by the FDA: June 27, 2012

Qsymia

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