FDA Panel Seeks More Warnings on Antidepressants
By **Otesa** Middleton
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WASHINGTON -- More warnings should be added to the labels of antidepressant drugs, alerting doctors and parents about links to suicide and violence in children taking the medicines, a federal panel said Monday.

The group of drug experts and psychiatrists convened by the Food and Drug Administration said the agency needs to quickly update the labels.

Monday's meeting is part of the FDA's overall review of the use of these drugs in children. The agency already planned to reconvene the panel in June to further discuss the issue and related clinical trials. The agency, which will make the final decision, typically follows the advice of its outside panels of experts.

Panel Chairman Dr. Matthew V. Rudorfer, associate director of treatment research at the federal National Institute of Mental Health, wants to give doctors and families more data while studies are analyzed in preparation for June's meeting.

"The warnings as they exist are not adequate or they are not taken seriously," he said.

Last October, the FDA released an advisory reminding doctors that suicide is inherent in major depression and that high-risk young patients should be closely monitored when antidepressants are first prescribed.

Monday the FDA asked the panel for feedback on Eli Lilly & Co.'s Prozac, Pfizer Inc.'s Zoloft, Forest Laboratories' Celexa, GlaxoSmithKline PLC's Paxil, Wyeth's Effexor, Akzo Nobel NV unit Organon Inc.'s Remeron and Bristol-Myers Squibb Co.'s Serzone.

The day-long meeting prompted 63 public speakers from around the nation, many offering personal stories of children who attempted or committed suicide or were involved in other forms of violence.

One speaker was Mark Taylor, a survivor of the 1999 Columbine High School shooting massacre in which one of young killers was on antidepressants. Mr. Taylor, now 20 years old, told the panel, "Thousands of Americans died because of these drugs. It is a shame and ought to be stopped today, not next week."

Like Mr. Taylor, the majority of speakers brought heart-wrenching stories of violence and implored the panel to put strong warnings on the drug labels.

Joe Pittman read a letter from his son, Chris, who killed his grandparents when he was 12 years old, while taking Zoloft.

"It made me hate everyone," wrote Chris, who is now 14 years old. "The voice echoing in my head told me to kill them. It was like watching my favorite TV show and knowing what is going to happen, but not being able to stop it."

However, the National Alliance for the Mentally Ill strongly urged the panel to give more weight to clinical trial data rather than personal anecdotes that offer circumstantial evidence against the drugs.

"Eighty percent of youth who need mental-health treatment don't receive it," said Suzanne Vogel-Scibilia, representing the 200,000-member group.

Rachel Adler, a board member of the Child and Adolescent Bipolar Foundation, supported use of the drugs.

"To blame the medication itself that has helped so many people, I don't think is the right way," Ms. Adler said.

Dr. Russell Katz, director of the FDA's division of neuropharmacological drug products, said the panel's recommendations were "very clear." To the families who told the agency and its panels their stories, Dr. Katz said, "We heard you."

FDA Approves Prozac Under New Name For Severe PMS
By **Otesa** Middleton
6 July 2000

WASHINGTON -(Dow Jones)- With a new name, new package and new use, Eli Lilly & Co.'s Prozac won federal approval Thursday as the first drug to treat severe moodiness and pain that accompany some women's monthly menstrual cycle.

The drug's chemical name, fluoxitine hydrochloride, remains the same. However, for treating premenstrual dysphoric disorder, the drug will be sold under the name Sarafem in blister packs of 28 pink and purple capsules - not in bottles of cream and green capsules like Prozac.

This strategy is to help differentiate this severe form of premenstrual syndrome, or PMS, from depression, said Laura Miller, a Lilly spokeswoman.

"Prozac is one of the best known trademarks for treating depression," Miller said.

Giving Sarafem a separate name and packaging to coincide with a woman's monthly menstrual cycle makes it more convenient and customized for this disorder, Miller said.

Each box of Sarafem will include patient information on the disorder and on how to use Sarafem, which should be available in pharmacies next month. Both Sarafem and Prozac wholesale for about $2 per pill.

Although Lilly will give the drug a separate look for this use, the name Prozac carries a lot of influence, said David Saks, pharmaceutical analyst at Gruntal & Co.

"My first inclination is to say the name Prozac has great value," Saks said. "However, Eli Lilly thought it better for it to have its own space and identity."

"Maybe it's because Prozac's patent is expiring in the next couple of years and coming out with a separate, stand-alone product has more bang than a just a new use of a great brand," Saks said.

Also, Saks said, winning new approvals for Prozac is part of Lilly's strategy.

"At a time when Prozac may be competing with generics in a few years, it may be better in the feminine market for it to have its own identity," he said.

Saks said he isn't certain about the sales impact of Sarafem because some women may already be taking Prozac or another similar drug for premenstrual dysphoric disorder. If a drug has federal approval to be sold in the U.S., doctors can prescribe it for any use. However, companies can only promote drugs for approved uses.

Prozac, which led a wave of new depression treatments when it was first approved by the Food and Drug Administration in December 1997, is also marketed in the U.S. as a treatment for obsessive compulsive disorder and bulimia. The drug, a selective serotonin reuptake inhibitor, had $2.6 billion in sales for 1999. Since it has been on the market, more than 38 million people around the world have taken Prozac, according to Lilly.

The FDA's approval of the drug for premenstrual dysphoric disorder was expected after a panel of agency advisors unanimously supported the drug in November.

Symptoms of the disorder occur between ovulation and onset of menstruation. The symptoms include depressed mood, anxiety, tension, alternating between cheerful and somber moods, persistent anger or irritability, decreased interest in activities, difficulty in concentrating, lack of energy, change in appetite, headache, joint and muscle pain, weight gain, bloating and breast tenderness.

FDA Panel Backs Prozac For Premenstrual Mood Disorder
By Otesa Middleton
3 November 1999

WASHINGTON -(Dow Jones)- A well-known drug may soon be the first approved to treat severe moodiness that plagues some women before their monthly period.

A federal panel urged the government to grant a new approval for Eli Lilly & Co.'s Prozac to treat premenstrual dysphoric disorder. The Food and Drug Administration is expected to follow the panel's advice when it rules on expanding the marketing clearance for the widely used drug.

If ultimately approved, Prozac sales aren't expected to significantly increase. However, winning a new indication for the established drug may strengthen its position, helping Prozac stave off competition and perhaps slowing the product's recent modest decline.

Prozac, which has been on the market for a decade, is already approved for treating depression, obsessive-compulsive disorder and bulimia. Still Lilly's top drug and the leading antidepressant, Prozac had $690 million in third-quarter sales, down 13% from the same period last year. By year's end, sales are expected to drop 5% to $2.68 billion.

More than 35 million patients worldwide have used the drug, a pioneer in **new** treatment options for depressive disorders. Prozac was the first in the class of drugs called selective serotonin reuptake inhibitors, a group that includes SmithKline Beecham PLC's Paxil and Pfizer Inc.'s Zoloft.

Again a pioneer, Prozac is the first drug reviewed by the FDA for treating premenstrual dysphoric disorder, although other drugs are being studied for this condition.

The disorder is considered a severe case of premenstrual syndrome. Up to 80% of women have PMS, which causes mild mood swings and breast tenderness before each period.

Only about 3% to 5% have premenstrual dysphoric disorder, which is characterized by severe moodiness, irritability, anxiety, depression, difficulty concentrating, lethargy, marked change in appetite, insomnia and a feeling of being overwhelmed.

Unlike PMS, the more severe disorder "markedly interferes with work, school, usual social activities and relationships," according to Dr. Jean Endicott of Columbia University's department of psychiatry.

"This is a chronic condition and the women have had it for years," Endicott told the panel on Lilly's behalf.

With this cyclical disorder, women show signs before each period and symptoms stop with pregnancy and menopause.

The FDA is expected to make its decision on the **new** Prozac approval by year's end.

The panel's unanimous support for Prozac makes it very likely the agency will grant Lilly's request.

The company presented the FDA panel with three studies, which were initiated and conducted by independent researchers. One six-month study of 400 women was designed to determine the correct Prozac dose for treating premenstrual dysphoric disorder.

The two other smaller, shorter studies looked at a total of almost 70 women.

Dr. Rajinder Judge, a Lilly medical director, said compared to a sugar pill, doses of 20 to 60 milligrams of Prozac were shown to significantly reduce symptoms. Symptoms subsided quickly after starting the medication. However, soon after Prozac therapy was stopped, symptoms returned.

The company recommends the 20 milligram dose, which produced fewer side effects and worked in most women. However, some women may need to try Prozac doses of up to 60 milligrams, Judge said.

Federal advisors agreed that the premenstrual dysphoric disorder is a diagnosable condition, but the group disagreed on whether PMS is a diagnosable disorder. The FDA asked the panel to help define the two conditions because the agency has no precedent on reviewing treatments for them.

Although this use probably won't cause Prozac's sales to surge, "every additional indication helps," according to Hambrecht & Quist pharmaceutical analyst Corey Davis.

Prozac's 15.3% market share among all antidepressants is slipping, Davis said, and any additional claim will give Lilly's sales force the upper hand when pitching the drug to doctors.

Although doctors can prescribe any approved drug for the disorder, the company can't promote a drug for an unapproved use without government clearance.

Neil Sweig, pharmaceutical analyst for Ryan, Beck/Southwest Research agreed.

"This is part of broadening the claims on the label," Sweig said. "This would increase the chances for the product to be used."

"We can assume the growth for Prozac is over, beginning this year," Sweig said. "Sales have been modestly declining."

For 2000, he projects Prozac's sales to dip another 3% to $2.6 billion. Sweig said the 10% growth the drug saw in 1998 was its last year to see an increase.

"The antidepressant market is overly crowded, which puts pressure on Prozac," Sweig said.

For premenstrual dysphoric disorder, Lilly has two other Prozac studies underway, each looking at 250 patients who are given the drug intermittently instead of every day.

Last month, the United Kingdom gave Lilly permission to market Prozac for premenstrual dysphoric disorder.

Depression Sufferers Express Dissatisfaction With Medication, Doctors
By **Otesa** Middleton, Staff Reporter
30 November 1999

WASHINGTON -(Dow Jones)- Most patients with depression want new, more effective medicines with fewer side effects, according to a new survey.

The online poll taken by the National Depressive and Manic-Depressive Association found 80% of patients said their depression impaired their social and family life in the last month, although they were taking prescriptions for the condition.

Also, 80% said they experienced side effects from their prescriptions, while 17% said the side effects caused them to stop using the drug.

Two thirds of the respondents said the relationship with their doctors was less than satisfactory. Half said they felt misunderstood.

The association released the results of the survey Tuesday. The poll, conducted on the group's Web site, questioned 1,370 people who had been treated for depression in the last five years.

Dr. Dennis Charney, deputy chairman and professor in Yale University School of Medicine's Department of Psychiatry, said the survey results signaled the need for more new antidepressants.

"In general, the drugs work very well. A lot of patients do get better," Charney said.

But for patients who continue to have symptoms, Charney said, "we need to do better."

Most of the more than 20 antidepressants available attack the same chemicals in the brain, he said.

"We need to discover new antidepressants that act differently in the brain and that aren't operating on the same systems," Charney said.

But he also said the survey may not be totally representative because people who answered chose to write and weren't randomly selected.

People who were feeling great may not have felt the need to write in, he said.

Charney said the survey's results were more negative than he expected.

"A surprising number of people felt their relationship with their treater wasn't optimal," Charney said. "That implies there is a need for greater education of the causes and treatment of depression."

More than 23 million Americans live with depression, according to the National Depressive and Manic-Depressive Association.

Lydia Lewis, the group's executive director, said the survey gives those suffering from **depression** a voice.

"While we know that treatment works for more than 80% of those suffering from a depressive illness, we still urgently need new strategies for managing depression," Lewis said. "The solutions lie in continued research and continued dialogue between patients and physicians."