Controversial disease dropped from Prozac product information

Ray Moynihan *Washington, DC*

The drug manufacturer Lilly has been forced to drop one of the disorders it had previously listed for its antidepressant drug fluoxetine (Prozac), following a finding by the European drug regulator that the condition was not a well-established disease entity.

Some health researchers welcomed the regulator's decision, saying premenstrual dysphoric disorder (PMDD), which was only recently described, was an invented illness and a strong example of the medicalisation of ordinary life.

"I think it's a wonderful decision" says Paula Caplan, a psychologist adjunct and professor at Brown University, Rhode Island. "This kind of scrutiny of the science or lack of science behind trials of drugs is all too rare and it is to be praised."

Lilly informed health professionals in a letter in December that it had removed premenstrual dysphoric disorder as an indication for fluoxetine, citing a ruling by the European drug regulator earlier in the year.

In June 2003, as part of European harmonisation of product information, the Committee for Proprietary Medicinal Products found that "PMDD is not a well-established disease entity across Europe." It said that the disorder was not listed in the international classification of diseases

and was listed only as a research diagnosis in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders*.

The committee strongly criticised two key trials of fluoxetine for premenstrual dysphoric disorder, noting that in one study almost half of the participants dropped out and that in the other little attempt was made to distinguish between mild and severe health problems. "There was considerable concern that women with less severe premenstrual symptoms might erroneously receive a diagnosis of PMDD resulting in widespread inappropriate short and long term use of fluoxetine," wrote the committee.

Fluoxetine was first approved for premenstrual dysphoric disorder by the US Food and Drug Administration in 2000, after an influential 1998 "round table discussion" of experts supported by Lilly and attended by at least four Lilly representatives. The disorder was characterised by anger, irritability, and tension triggered by the menstrual cycle.

An aggressive promotional campaign quickly followed, including television advertisements featuring a frustrated woman with a shopping trolley outside a shop and accompanied by the line, "Think its PMS [premenstrual syndrome]? It could be PMDD." The campaign was

South African doctors march in protest

About 2000 doctors employed in the public and private sector marched through the streets of Cape Town when the South African parliament started last week. They were protesting about several new measures that they say are forcing doctors to quit the country in growing numbers.

The measures include stopping doctors dispensing drugs (about 6000 doctors dispense at present), forcing them to get a "certificate of need" in order to open a practice in a specific area, and changes in reimbursement in health insurance. They were also protesting about basic pay and working conditions in the private sector. The march was led by the South African Medical Association.

Pat Sidney *Johannesburg*

criticised by some women's groups and was found by the Food and Drug Administration to be unbalanced and misleading because it "broadens the indication" and played down side effects (<http://www.fda.gov/cder/warn/nov2000/dd9523.pdf>).

In 2001, based on the work of Caplan and others, the Society for Menstrual Cycle Research called on the administration to overturn its approval of fluoxetine for the disorder, asserting

that the condition did not exist and widespread use of the drug for menstrual problems could mask other causes of women's suffering. Instead the regulator has gone on to approve a number of other antidepressants for the disorder.

A spokesperson for Lilly said company officials understood the European regulator's decision, but thought it "unfortunate". □

Follow up for childhood cancer survivors needs clarification

Owen Dyer *London*

Cancer Research UK has called for guidelines on the long term follow up of survivors of childhood cancer, after a study commissioned by the charity found extensive variation in the way these patients are monitored in later life.

Survival prospects in most childhood cancers have been improving for decades, with the result that long term survivors today make up about 1 in 1000 of the adult population. Some

estimates suggest that up to 70% will develop late adverse health outcomes relating to their cancer treatment, including cardiac and endocrine problems. A team of researchers from several hospitals questioned specialists and GPs about these patients' follow up on behalf of the Late Effects Group of the United Kingdom Children's Cancer Study Group (UKCCSG).

The researchers questioned clinicians who treated patients in

the ongoing British childhood cancer survivor study, a population based cohort study of 14 392 survivors of childhood cancer in Britain who are aged at least 16 years. It is published in the current issue of the journal *Pediatric Blood and Cancer* (2004; 42:161-8).

According to the GPs of 10 979 childhood cancer survivors, 65% of these patients are no longer on regular long term hospital follow up. The trend, however, is towards more follow up. Among the most recent cohort of patients, who were treated as paediatric patients for cancer in 1990-1, 63% are still receiving follow up, compared with only 9% of those whose dis-

ease was treated in the 1950s.

Overall, 97% of 71 specialist clinicians questioned said they followed up paediatric cancer patients for at least five years. After five years, 52% of the clinicians continued to follow up all their patients for life, but 45% discharged some of their patients, nearly always to the patient's GP.

The authors do not speculate on whether patients are at risk due to insufficient follow up, partly because no clear picture exists of the real late effects of childhood cancer and its successful treatment. A review of evidence on late effects should be published soon by the Scottish Intercollegiate Guidelines Network. □