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Smoking-pill suicides overlooked in missing reports

Drugmaker sent data through 'improper channels;'FDA didn't have full picture of

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Hundreds of reports of suicides, psychotic reactions and other serious problems tied to the popular stop-smoking drug Chantix were left out of a crucial government safety review because Pfizer Inc., the drug's manufacturer, submitted years of data through "improper channels."

Some 150 suicides — more than doubling those previously known — were among 589 delayed reports of severe issues turned up in a new analysis by the non-profit Institute for Safe Medication Practices.

"We've had a major breakdown in safety surveillance," said Thomas J. Moore, the ISMP senior scientist who analyzed the data. The serious problems — including reports of completed suicides, suicide attempts, aggression and hostility and depression — had been mixed among some 26,000 records of n on-serious side effects such as nausea and rashes, with some dating back to 2006, the year Chantix, or varenicline, was approved.

They echo previous claims that the drug can induce extreme reactions in people trying to quit cigarettes, including vivid nightmares, crippling depression and sudden, violent outbursts.

"It's really chilling," said Moore, who analyzed 26 Chantix reactions in a paper published in the September 2010 issue of the Journal of Pharmacotherapy. "This seems to unleash something in people. It can be violence to anything around."

Moore's case studies describe "inexplicable and unprovoked" reactions in Chantix patients with no previous history of violence or mental illness, including:

- A 24-year-old woman who started beating her boyfriend in bed because "he looked so peaceful" and later attempted suicide;
- A 42-year-old man who punched a stranger at a bowling alley;
- A 47-year-old woman who died after she came out of a room, yelled at her daughters and then shot herself.

Federal Food and Drug Administration officials acknowledged that they asked Pfizer to resubmit thousands of records after realizing that the company was sending required reports in an inappropriate format that could

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not be added to the agency's Adverse Events Reporting System, or AERS.

"Last year, FDA became aware that a few manufacturers were submitting adverse events reports to FDA through improper channels," the agency said in a statement.

Pfizer officials said they were submitting reports as required and that when the FDA asked them to change, they did so immediately. They said there's no proof that Chantix causes suicide or other serious side effects.

Moore, who has served as an expert witness in court regarding Chantix, said it's the riskiest drug among those analyzed from the FDA's adverse event reports. In the third quarter of 2010, it ranked first in reported deaths, with twice as many fatalities logged as any other drug, he said.

New reports don't change FDA's position

FDA officials said the new reports did not change the agency's position on the risks and benefits of the controversial drug, which received a black box warning that included suicide — the strongest caution possible — in 2009, according to agency officials who would not speak on the record.

"At this point, based on the data, FDA does not have any new safety concerns with Chantix, though those that have been established remain under active review," the agency said in a statement posted in response to the ISMP report.

Agency officials said they're continuing to review Chantix in clinical trials and two large observational studies with the Veterans Administration and the Department of Defense.

But Moore said the new data should raise immediate alarms about the drug that was prescribed 3.2 million times last year to people trying to stop smoking — and 1.1 million times already this year, according to data from the firm Wolters Kluwer Pharma Solutions.

"To us, it raises questions about whether this drug is safe for widespread clinical use," Moore said. "Does this tip the balance?"

That's a view echoed by families of people who allegedly became suddenly and inexplicably violent after taking Chantix. Sean M. Wain, 34, of Beaver County, Pa., shot himself and his wife, Natalie, 33, in May 2009 in what a lawyer for their families claims was a Chantix-fueled rage.

If the FDA had more information about suicides and other side effects tied to Chantix, the agency might have taken stronger action sooner, said Victor H. Prebanic, who represents Robert Erdelen and George Wain, fathers of the slain couple.

"If Pfizer had been more forthcoming, the black box warning might have emerged earlier," Prebanic said. "For all we know, the drug would not have been available."

The lawsuit, filed this month, is the latest among hundreds of claims filed against Pfizer regarding Chantix. At least 1,545 injury claims that cite Chantix are pending in federal court.

Pfizer officials, however, said that the firm was following the FDA's rules and changed their reporting process once the agency asked for clarification.

"All post-marketing reports of adverse events are reviewed by Pfizer and reported to regulators, including FDA, in accordance with

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regulatory guidelines," the company said in a statement. "Pfizer takes patient safety and regulatory reporting obligations very seriously."

Suicide is an 'expected' event?

The problem appears to have been caused in part by federal Food and Drug Administration rules that don't require firms to submit new reports of death or serious harm in the agency's system for urgent review when such risks are already known.

FDA requires drugmakers to submit adverse events in two ways: There's an "expedited" system that requires companies to report serious and unexpected adverse events into the AERS system within 15 days.

Companies are also required to submit less-serious and expected adverse events quarterly in so-called "periodic reports." In those cases, problems previously included on drug labels — including suicide and suicide attempts — are considered to be expected events.

In Pfizer's case, the firm was submitting the periodic reports as required, but combining summaries and individual case reports in a single text file, the FDA said.

That meant that the individual reports of injury were not logged in the FDA's AERS system, drastically reducing known reports of suicides and other psychiatric problems tied to Chantix, Moore said.

"It's very clear the suicide risk of this drug was higher than we knew," he said.

Overall, there were 1,055 reports of serious problems with Chantix reported in the third quarter of 2010, more than any other prescription medication regularly monitored by the drug safety agency, Moore said.

Before last July, the FDA had logged 122 reports of suicides linked to Chantix, including 37 reported by Pfizer and 85 reported by health professionals or consumers, Moore reported. After the 150 new Pfizer reports were added, the total jumped to 272.

In addition, the 589 new reports of severe problems included 102 cases of possible hostility and aggression, 156 cases of depression and 56 cases of possible psychosis. Those were mixed among the 26,000 reports of less-serious problems.

Moore has asked the FDA to investigate the 150 new suicide reports, particularly if the events occurred before the 2009 black box warning listed suicide as a possible side effect.

For their part, FDA officials said they are considering changing regulations to allow expedited reports of suicides and other serious problems, even if they've previously been identified as expected. First proposed in 2003, that change is still pending.

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