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Heart Warning Added to Label on Popular Antipsychotic Drug

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AstraZeneca is adding a new heart warning to the labels of Seroquel, its blockbuster antipsychotic drug, at the request of the Food and Drug Administration, company and agency officials said on Monday.

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Warnings for Seroquel will soon recommend that the drug be avoided in combination with 12 drugs linked to arrhythmia.

The revised label, posted without fanfare last week on the F.D.A. Web site, says Seroquel and extended-release Seroquel XR "should be avoided" in combination with at least 12 other medicines linked to a heart arrhythmia that can cause sudden cardiac arrest.

Sandy Walsh, a spokeswoman for the F.D.A., said the statement was only a precaution for doctors, and should not be considered a complete ban against prescribing Seroquel with the other drugs.

Ms. Walsh said the label was changed after the F.D.A. received new information about reports of arrhythmia in 17 people who took more than the recommended doses of Seroquel. Though it should not be a problem at a normal dosage, she said, it may still be good advice to avoid using the drugs together.

The arrhythmia, known as prolongation of the QT interval, referring to two waves of the heart's electrical rhythm, is estimated to cause several thousand deaths a year in the United States.

As AstraZeneca prepares to report its second-quarter earnings at the end of this month, it faces additional scrutiny this week. The F.D.A. is considering the London-based company's dapagliflozin, a proposed diabetes drug with Bristol-Myers Squibb, and is expected to decide soon on Brilinta, an anticoagulant. The company is facing the loss of patents for Seroquel next year and for the heartburn drug Nexium in 2014.

Seroquel is one of the top-selling drugs in the world, at $5.3 billion last year, including $3.7 billion in the United States. Introduced in 1997, it has been approved for schizophrenia, bipolar disorder and severe depression. Seroquel has caused legal problems for AstraZeneca, including a $520 million payment in 2009 to settle government charges of illegal marketing. Thousands of lawsuits are pending over side effects like diabetes.

The previous Seroquel labels had mentioned the risk of a prolonged QT interval, but had not identified other drugs to avoid, Stephanie Andrzejewski, a spokeswoman for AstraZeneca, said Monday. The new warning also is separated from other warnings and precautions on the label, she said, "to provide some additional guidance to physicians" treating patients "who are already at risk of QT prolongation."

The new warning will be added to printed labels as soon as possible, Ms. Andrzejewski said.

The new label lists the other drugs to avoid as antiarrhythmic drugs like quinidine, procainamide, amiodarone and sotalel; antipsychotic drugs like ziprasidone, chlorpromazine and thioridazine; antibiotics like gatifloxacin and moxifloxacin; the anti-infective drug pentamidine; and synthetic opioids like levomethadyl acetate and methadone. The label also raises caution about use by the aged and people with heart disease.

James J. Pepper, a lawyer in Pennsylvania who is involved in drug litigation, has been arguing for months in letters to government officials that Seroquel has a potentially deadly interaction with methadone in regard to the QT interval.

"This is a huge, huge step," Mr. Pepper said of the label change, though he said he thought it should be stronger.

Ms. Walsh said the F.D.A. action was unrelated to Mr. Pepper's arguments.

Three months ago, Dr. Janet Woodcock, director of the F.D.A. Center for Drug Evaluation and Research, rejected those arguments in a letter to the Project on Government Oversight, a nonprofit group in Washington, which had also raised the issues. Dr. Woodcock wrote that a thorough agency review had found it "exceedingly unlikely" that patients faced an unreasonable risk from the interaction between Seroquel and methadone. The review found only one death that was probably caused by the interaction, she wrote.

Dr. Woodcock concluded that the F.D.A. would take no action to change the label. Ms. Walsh said that conclusion was still correct, because the F.D.A. had found no biological basis for a problem or unusual numbers of deaths at normal dosages.

Methadone use and deaths have increased drastically in recent years as more doctors prescribe it for chronic pain. The number of methadone prescriptions for pain in the United States rose to 4.3 million in 2010 from 2.2 million in 2006, IMS Health, an industry data firm, said Monday. The use for pain has surpassed that for heroin withdrawal and maintenance.

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